SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Hernia Mesh Fixation Device

Device Trade Name: LiquiFix FIX8™ Hernia Mesh Fixation device.
LiquiFix Precision™ Open Hernia Mesh Fixation device.

Device Procode: PLJ

Applicant's Name and Address: Advanced Medical Solutions Limited, Western Wood Way, Langage Science Park, Plymouth, Devon, UK, PL7 5BG

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P220024

Date of FDA Notice of Approval: June 2, 2023

II. INDICATIONS FOR USE

LIQUIFIX FIX8™
The LIQUIFIX FIX8™ Hernia Mesh Fixation device is intended for use in laparoscopic surgical repair of groin (inguinal and femoral) hernias, achieved through the fixation of prosthetic polypropylene or polyester mesh to the abdominal wall and the approximation of the peritoneum.

LIQUIFIX Precision™ Open
The LIQUIFIX Precision™ Open Hernia Mesh Fixation device is intended for use in open surgical repair of groin (inguinal and femoral) hernias, achieved through the fixation of prosthetic polypropylene or polyester mesh to the abdominal wall.

III. CONTRAINDICATIONS

- The device is not intended for use when prosthetic material fixation is contraindicated.
- Do not use on patients with a hypersensitivity to cyanoacrylate adhesives, formaldehyde, or D&C Violet No. 2 dye
- Do not use for the fixation of meshes constructed with polytetrafluoroethylene (PTFE). or materials other than polypropylene or polyester.
- Do not use device for closure or fixation of cerebral tissues, blood vessels or peripheral nerves.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the LIQUIFIX labeling. Specific warning for use of LiquiFix in anchoring mesh in open inguinal hernia repair will restrict its use of application directly on the mesh positioned as an onlay on the floor of the inguinal canal, as in a Lichtenstein repair or with use of mesh to reinforce a primary repair.

V. DEVICE DESCRIPTION

The LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open Hernia Mesh Fixation devices are designed for the application of an n-butyl-2- cyanoacrylate adhesive to an implanted hernia repair mesh, in order to affix the mesh to the underlying tissue. Additionally, the device may be used for tissue-to-tissue approximation of the peritoneum (LIQUIFIX FIX8™ Laparoscopic Hernia Mesh Fixation device). The adhesive is non- bioabsorbable and becomes encapsulated within the body, along with the hernia mesh. A representative image of the hernia mesh fixation devices is provided in Figure 1-2.

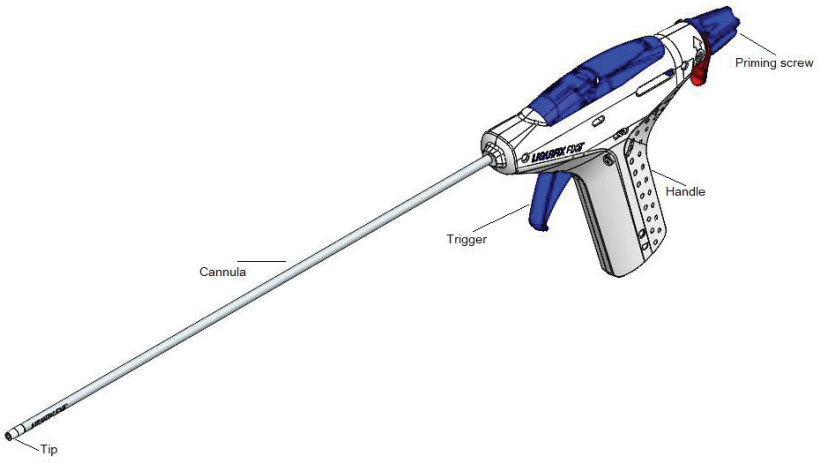

Figure 1: LIQUIFIX FIX8™ Laparo Hernia Mesh Fixation device

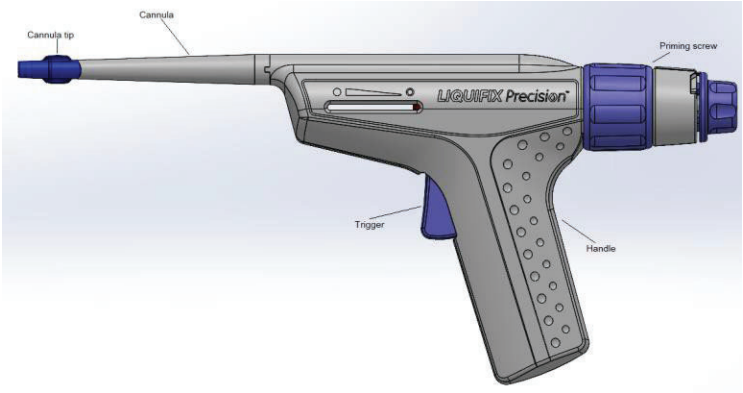

Figure 2: LIQUIFIX Precision™ Open Hernia Mesh Fixation device

Device Composition/Key Components/Materials

The LIQUIFIX Hernia Mesh Fixation devices consist of:

- n-butyl-2-cyanoacrylate adhesive monomer (cyanoacrylate adhesive), in liquid form, supplied in a thin-walled, sealed glass vial; and
- a surgically invasive, delivery instrument comprising a cannula, with a handle at the proximal end incorporating a loading chamber, filter, piston chamber and trigger. The distal tip of the device is open to allow the adhesive to be dispensed from it.

Both the cyanoacrylate adhesive in the glass vial and the surgically invasive delivery device are supplied sterile, for single use only. The device releases a drop of adhesive (anchor) when the trigger is pulled and released, which polymerizes on contact with tissue or moisture.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternative practices for the correction of groin (inguinal and femoral) hernia, which can be divided into non-surgical and surgical treatment. Usually if the hernia has no symptoms, a conservative non-surgical approach and watchful waiting may be an option. Conservative treatment of hernias includes the use of a corset, truss, or a belt, which applies pressure at the site. Surgical options include tissue approximation repairs (non-mesh repairs) with sutures at the site of the weakness or defect. In addition, a tension-free hernia repair using hernia mesh may be performed either laparoscopically or via open hernia repair using conventional mechanical fasteners such as metallic or absorbable tacks, sutures or staples. Adhesives, either synthetic adhesives such as cyanoacrylate, or biological products such as fibrin glue, have been introduced as an option for mesh fixation since this approach eliminates direct nerve irritation and nerve entrapment due to their atraumatic nature. Alternatively, absorbable microhooks on the fascia-facing side of mesh which induce a "self-gripping" property, negates any additional type of fixation.

For closure of the peritoneum during laparoscopic TAPP hernia repair, the peritoneum may be closed with several traditional closure techniques including sutures, tacks, and staples. Following closure of the peritoneum, standard practices and procedures are used for the subsequent closure of the fascial defect and skin.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The LIQUIFIX FIX8™ Laparoscopic Hernia Mesh Fixation device has been commercially available outside the United States (under brand name LiquiBand FIX8® Laparo) since 2014

for use in the laparoscopic surgical repair of inguinal and ventral incisional hernias, achieved through the fixation of prosthetic mesh to the abdominal wall and the approximation of the peritoneum. The product is currently distributed globally including regions such as Europe, Latin America, North America (Canada), Asia and Pacific and Middle East, as detailed in Table 1 below.

Table 1: Countries where the CE-marked version of Laparoscopic Hernia Mesh Fixation device has been marketed

Argentina	Israel	Singapore
Armenia	Malaysia	Taiwan
Australia	Mexico	Ukraine
Canada	New Zealand	United Arab Emirates
Costa Rica	Peru	United Kingdom
Ecuador	Saudi Arabia	Philippines
EU	Serbia	Sri Lanka
India		Republic of Korea

The LIQUIFIX Precision™ Open Hernia Mesh Fixation device has been commercially available outside the United States since 2018. The product is currently distributed globally including regions such as Europe, Latin America, North America (Canada), Asia and Pacific and Middle East. There has been one Outside US voluntary recall for the LiquiBand FIX8® Open device in January 2022 due to a mechanical device defect observed during internal testing of the device, and the device was modified to improve the seal tolerance, and verification completed. The recall has been closed and device made available.

Table 2: Countries where the CE-marked version of Open Hernia Mesh Fixation device has been marketed

Australia	India	Philippines
Brazil	Israel	Malaysia
Canada	New Zealand	Singapore
Ecuador	Saudi Arabia	Mexico
EU	Ukraine	United Kingdom

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open. The adverse events associated with the device are similar to those of traditional surgical hernia repair procedures.

As with the majority of implanted devices, adverse reactions associated with the use of this device may include transient local irritation at the implant site and a transitory inflammatory foreign body response. Advanced Medical Solutions has determined the potential adverse effects

(e.g., complications) listed below may be associated with the use of the LIQUIFIX devices. These potential adverse events include, but are not limited to, the following:

- Toxic reaction
- Allergic reaction

Clinical studies of LIQUIFIX adhesive using the Laparoscopic model of the device have been conducted inside and outside the United States. Adverse events observed during the US pivotal study have been described below; a number of these adverse events were possibly device related and possibly/definitely related to the procedure. In addition, adverse events observed during the four LiquiBand FIX8® (identical to LIQUIFIX FIX8™ except labelling) inguinal/femoral hernia repair European clinical studies, but not necessarily related to the device itself, included the following:

- Chronic Pain
- Hernia Recurrence
- Seroma
- Hematoma
- Swelling
- Neuralgia / Hypoesthesia
- Groin/ Testicular pain
- Intestinal obstruction
- Genital hemorrhage
- Spermatic Cord Inflammation
- Orchitis
- Lymphadenitis
- Mesh infection
- Urinary Retention
- Minor Surgical Emphysema
- Port Site Hernia
- Port Site Hemorrhage
- Inadvertent enterotomy
- Intra peritoneal bleeding
- Post-operative ileus
- Urinary bladder injury

Due to the identical adhesive, the adverse events are considered applicable to the LIQUIFIX Precision™ Open Hernia Mesh Fixation device as well.

For the specific adverse events that occurred in the clinical studies, please see Section X Summary of Primary Clinical Study below.

IX. SUMMARY OF NONCLINICAL STUDIES

A variety of non-clinical testing was performed with the LIQUIFIX FIX8™ device and the LIQUIFIX Precision™ Open device.

A summary of testing has been provided in Table 3 below.

A. Laboratory Studies

A brief summary of adhesive key performance specifications for both LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open conducted via bench top studies has been provided below. Device testing for LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open has been performed and passed.

Table 3: Laboratory Studies - LIQUIFIX adhesive

Test	Purpose
Material Characterization	
Set Time	This test evaluates: • Set time for adhesive polymerization (pre-sterile, post-sterile and aged adhesive) on salt solution. • Set time for mesh fixation. • Set time under different environmental conditions (saturated and dry conditions).
Tensile Strength – Lap Shear (mesh-to-tissue)	This test evaluates lap shear strength (ASTM F2255) of adhesive with hernia meshes.
Tensile Strength – T Peel	This test evaluates T-peel tensile strength (ASTM 2256) of adhesive attachment of mesh to tissue.
Viscosity	This test evaluates viscosity (cP) of the adhesive in comparison to other marketed cyanoacrylates.
Heat Polymerization	This test evaluates the heat of polymerization of adhesive on porcine tissue.
LIQUIFIX Applicator Testing	
Crush Force (LIQUIFIX FIX8™ model)	This test evaluates crush force of the crush cover of the device (required during priming) using a tensile test machine.
Torsional Loading (tip rotation) (LIQUIFIX FIX8™ model)	This test evaluates torsional loading of the shaft of the device using a torque meter until failure.
Tip Loading (tip deflection) (LIQUIFIX FIX8™ model)	This test evaluates tip deflection of the device after 50mm deflection.
Anchor size	This test evaluates average weight of the adhesive anchor (drop) after expression from the applicator device.
Dispense rate(LIQUIFIX FIX8™ model)	This test evaluates the average time taken to deploy a single adhesive anchor (following ten adhesive drops).
Dispense Angle (LIQUIFIX FIX8™ model)	This test evaluates the ability of the applicator to dispense adhesive at the clinically relevant angles.

Back pressure(LIQUIFIX FIX8™ model)	This test evaluates the performance of the device under pressure (within a pressurized vessel).
Insertion (LIQUIFIX FIX8™ model)	This test evaluates any drop in pressure.
Performance time	This test evaluates the ability of the device to dispense adhesive after 3±0.5 hours.
Anchor quantity	This test evaluates the total number of drops (adhesive anchor) a device can deliver.
Device	This test evaluates the device through visual inspection.
Device Leak (LIQUIFIX Precision™ model)	This test evaluates device leak when at rest in all orientations.
Adhesive gauge (LIQUIFIX Precision™ model)	This test evaluates gauge movement with every adhesive anchor delivered.
Ability to crack glass ampoule (LIQUIFIX Precision™ model)	This test evaluates the ability of the user to turn the ampoule plunger clockwise to break glass ampoule.

B. Animal Studies

Pre-clinical testing was performed in porcine and rabbit models to evaluate the safety and effectiveness of the LIQUIFIX adhesive and LIQUIFIX FIX8™ device (Table 4). The definitive animal studies support that the LIQUIFIX adhesive performs as intended.

Table 4: Results of unpublished animal studies

Test	Purpose	
Pilot Study: Porcine evaluation of the feasibility of the LIQUIFIX FIX8™ device for the surgical repair of hernia mesh and the closure of the peritoneum.	Early feasibility study to assess the performance of LIQUIFIX FIX8™ in vivo in three Swine.	The LIQUIFIX adhesive was found to provide fixation of adequate tensile strength to fix mesh within the pilot porcine study. No apparent mesh migration was observed at the day 14 time-point. Macroscopic and histological analysis 2 weeks post- fixation revealed a significant level of fibrosis and integration of the mesh into surrounding tissues. No adverse irritation or inflammation of the graft site was observed beyond what is typically expected following implantation of a foreign body.

Definitive study: Evaluation of LIQUIFIX FIX8™ in an Abdominal Wall Incision Model in Swine, 2 and 4 weeks.	Definitive study to evaluate the local effects and adhesion formation of LIQUIFIX FIX8™ when applied to abdominal wall incisions of the peritoneum in swine. Incisions in the peritoneum of the ventro-lateral abdominal wall were closed with either LIQUIFIX FIX8™ or polypropylene suture.	Under the conditions of this study, LIQUIFIX FIX8™ was considered to elicit a slight reaction in the tissue as compared to the control article (polypropylene suture), at 2- and 4- weeks following closure of the peritoneum of the pig. The sites were macroscopically normal. The additional evaluation of the left iliac vein and genital branch of the genitofemoral nerve, when exposed to the test article, resulted in no microscopic evidence of tissue injury at the sites when polymerized article was peeled away from nerve and vein tissue of freshly euthanized animals.
Definitive study: Evaluation of LIQUIFIX FIX8™ Laparoscopic in a Rabbit Abdominal Wall Defect Model - 2, 4, and 13 Weeks	An abdominal midline ventral incision was created to adequately expose the peritoneal surface of the abdominal wall in New Zealand White rabbits. LIQUIFIX FIX8™, and comparative control article, non- absorbable suture, were then used to fix the hernia mesh to the abdominal wall.	Under the conditions of this study, LIQUIFIX FIX8™ was considered to elicit minimal or no reaction in the tissue as compared to the comparative control article (polypropylene suture) when implanted in the abdominal wall of rabbits for 2, 4 and 13 weeks.

C. Additional Studies

1. Biocompatibility

Biocompatibility testing of the LIQUIFIX adhesive in its polymerized form and over the course of its polymerization reaction was performed. The applicator device materials which contact the patient or the adhesive pathway were also assessed for each device (LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open).

Table 5 briefly summarizes the testing performed on LIQUIFIX adhesive. In addition, chemical characterization of the adhesive was performed. The tests demonstrated appropriate biocompatibility, chemical characterization, and physical/chemical characterization.

Table 5: Results of Biocompatibility Testing – LIQUIFIX adhesive (pre-polymerized, in situ polymerizing and polymerized state)

Biological Endpoint	Study Type
Cytotoxicity	Cytotoxicity MTT ISO 10993-5
Sensitization	Kligman Maximization ISO 10993-10
Irritation	Intracutaneous Injection ISO 10993-10
Acute Toxicity	Acute Systemic Injection ISO 10993-11
Systemic Toxicity	Systemic Toxicity by subcutaneous Implantation – 28 days ISO 10993-11
Systemic Toxicity	Systemic Toxicity by subcutaneous Implantation – 90 days ISO 10993-11
Genotoxicity	Reverse Mutation Assay ISO 10993-3
Genotoxicity	Mouse Lymphoma Mutagenesis Assay ISO 10993-3
Genotoxicity	Rodent Blood Micronucleus Assay ISO 10993-3
Implantation effects	Intramuscular Implantation – 4 weeks ISO 10993-6
Implantation effects	Intramuscular Implantation – 13 weeks ISO 10993-6
Material Mediated Pyrogen	Material Mediated Pyrogen ISO 10993-11
Chemical Characterization: Interaction between adhesive and mesh. Polymerization of adhesive. Potential hydrolytic degradation.	Chemical Characterization ISO 10993-12 ISO 10993-18
Physical/ chemical characterization	EN 14477

The following testing was performed on the LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open device applicator components which make direct/indirect contact with the patient:

- Cytotoxicity (Cytotoxicity Elution Method ISO 10993-5 / Cytotoxicity MTS)
- Irritation (Intracutaneous Injection ISO 10993-10)
- Sensitization (Kligman Maximization ISO 10993-10)
- Extraction Study (Chemical Characterization EN ISO 10993-12, EN ISO 10993-18)

The LIQUIFIX Hernia Mesh Fixation devices are considered to meet the requirements of ISO 10993-1 for its intended use, and so can be considered biologically safe.

2. Sterilization

The LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open Hernia Mesh Fixation devices are supplied sterile. The devices are sterilized using both electron beam (e-beam) irradiation and ethylene oxide (EO) to a sterility assurance level (SAL) of 10-6.

3. Packaging Validation

The results of the ISTA 3a transit testing performed with final packaged LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open devices deemed that the device was successfully validated in the transit study.

4. Shelf-Life Validation

At interim and end of shelf life timepoints, product was evaluated for conformance with functional performance specification and adhesive specification. Conformance with the tested specifications was confirmed at the end of shelf life. Real time stability data available at the time of PMA approval establishes a shelf life of 18 months for LIQUIFIX Hernia Mesh Fixation Devices.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The clinical evidence supporting the safety and effectiveness of the LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open devices is derived from a combination of a US clinical IDE study and Outside-US clinical studies and post market surveillance (real world evidence).

The Applicant performed a clinical study under the IDE pathway to establish a reasonable assurance of safety and effectiveness of the surgical repair of groin (inguinal and femoral) hernias, achieved through the fixation of prosthetic mesh to the abdominal wall and the approximation of peritoneum in the US under IDE G190018. Data from this clinical study were the basis for the PMA decision, as well as additional foreign (OUS) clinical data supporting the US clinical data.

Pivotal Clinical Study (LBF8-01 Clinical Evaluation of LIQUIFIX FIX8™)

A. Study Design

The safety and effectiveness of LIQUIFIX FIX8™ is derived from one US pivotal study and several clinical studies performed outside-US. The US pivotal study has been summarized below.

A prospective randomized, controlled, single blinded, parallel-group, IDE non-inferiority study was conducted to evaluate the clinical performance and safety of LIQUIFIX FIX8™ versus control (absorbable tacker) for hernia mesh fixation and peritoneal closure in groin (inguinal and femoral) hernia repair. Two hundred and eighty-four (284) patients from five (5) investigational sites across the USA were enrolled in the study. 186 patients underwent Transabdominal preperitoneal repairs (TAPP) and 98 patients underwent Totally Extraperitoneal repairs (TEP) equally divided into the two experimental groups for each surgical approach.

The primary endpoint of improvement in pain is evaluated at the 6-month visit and measures the reduction of recorded Visual Analog Scale (VAS) since baseline (worst pain experienced within 1 month of screening visit). Following discharge, study subjects entered the follow-up period consisting of in-clinic and remote visits to assess primary endpoint of improvement in pain not inferior to control device as measured by a VAS value (0 = no pain to 10 = most pain imaginable) from baseline (worst pain experienced within 1 month of screening visit) to six months post hernia repair. The secondary endpoints of mesh fixation and peritoneal closure (Trans abdominal preperitoneal (TAPP) repairs only) were assessed at time of surgery. Following discharge, study subjects entered the follow-up period consisting of in-clinic and remote visits to assess the secondary endpoints of pain experienced, quality of life as well as the incidence of hernia recurrence and adverse events. Follow-up visits were performed at discharge and then post-operatively at week 1, week 2, month 1, month 3, month 6, month 9 and month 12.

The secondary endpoints were:

- To evaluate the incidence of hernia recurrence in patients following laparoscopic (Totally Extraperitoneal (TEP) and TAPP) hernia repair using LIQUIFIX FIX8™ or control device.
- To compare the use of LIQUIFIX FIX8™ to control device for mesh fixation at time of surgery.
- To compare the use of LIQUIFIX FIX8™ to control devices for the approximation of the peritoneum (TAPP repairs only) at time of surgery.
- To evaluate the quality of life experienced by subjects following groin hernia repair by LIQUIFIX FIX8™ or control as measured by the Carolinas Comfort Scale (CCS) at baseline (prior to surgery), and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months, and 12 months following surgery.
- To compare levels of pain experienced following laparoscopic (TEP and TAPP) groin hernia repair by LIQUIFIX FIX8™ or control device, as measured by VAS at discharge, and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months, and 12 months following surgery.

- To evaluate the safety of LIQUIFIX FIX8™ and control device for groin hernia repair by comparing incidence of adverse events in patients post laparoscopic groin hernia repair.

The control group is an FDA-cleared tacker device with similar indications for use, AbsorbaTack™ 5mm Absorbable Fixation Device (Medtronic/Covidien). AbsorbaTack™ is intended for fixation of prosthetic material to soft tissue in various minimally invasive and open surgical procedures such as hernia repair.

A total of 284 patients had their surgical procedure performed between August 22, 2019 and December 03, 2021 (LIQUIFIX FIX8™ n=142; AbsorbaTack™ n=142). The data for this PMA reflected complete data collected through to January 23, 2023.

At 6-month follow-up, out of 284 randomized patients, 282 were eligible (Eligible: Last Follow-up date > Visit 6 Window Open date), clinical follow-up was performed in 269 patients (136 LIQUIFIX FIX8™, 133 AbsorbaTack™). At 6-month follow-up, seven patients (5 LIQUIFIX FIX8™, 2 AbsorbaTack™) were lost-to-follow-up with their last visit occurring prior to Month 6, and six patients (1 LIQUIFIX FIX8™, 5 AbsorbaTack™) missed the 6-month visit, but had completed the study. The other 2 patients were ineligible; one patient (control) was lost to follow up and one patient (control) withdrew consent.

At 12-month follow-up, out of 284 randomized patients, 276 were eligible (Eligible: Last Follow-up date > Visit 12 Window Open date), 266 patients completed clinical follow-up (132 LIQUIFIX FIX8™; 134 AbsorbaTack™). At 12 month follow-up, 10 patients (6 LIQUIFIX FIX8™, 4 AbsorbaTack™) were lost to follow-up. 1 patient experienced an SAE that prevented attending all study visits and was deemed not eligible for 12 month visit because their study exit date was prior to the Month 12 Visit Window opening. Note, their study exit was assigned to the 12-month column because their study exit date was after the Month 9 visit closed. The other 7 patients were ineligible; six patients (2 LIQUIFIX FIX8™, 4 AbsorbaTack™) were lost to follow up and one patient (AbsorbaTack™) withdrew consent.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the LBF8-01 study was limited to patients who met the following inclusion criteria:

1) Is male or female, ≥22 years of age.
2) Is willing and able to give written informed consent.
3) Has a primary or recurrent groin hernia (unilateral or bilateral, inguinal or femoral).
4) Is currently scheduled and eligible for TAPP or TEP laparoscopic groin hernia repair (inguinal or femoral).
5) Hernia mesh to be used at the time of surgery is at least 4” x 6” in size and is one of the following:

   a. 3D Max™ Mesh (Bard Inc.)
   b. 3D Max™ Light (Bard Inc.)

c. Parietex™ 2D (order code starting with TEC) Flat Sheet Mesh (Medtronic)
d. Parietex™ 3D (order code starting with TET) Flat Sheet Mesh (Medtronic)

6) Is willing and able to comply with the protocol assessments at time of surgery and during the post-surgical follow up period.

Patients were not permitted to enroll in the LBF8-01 study if they met any of the following exclusion criteria:

1) Has a hernia type not suitable for laparoscopic hernia repair as determined by the Investigator (i.e., strangulated).
2) Subject has a recurrent groin hernia previously repaired laparoscopically, has an anatomical defect or had prior surgical procedures that in the opinion of the Investigator prevents access to the pre-peritoneal space for TAPP or TEP laparoscopic hernia repair
3) Is pregnant or actively breastfeeding.
4) Has a known sensitivity to cyanoacrylate or formaldehyde, D&C Violet No.2 dye or any component of LIQUIFIX FIX8™ or control device.
5) Has an active or potential infection at the surgical site or systemic sepsis.
6) Hernia mesh to be used at surgery is less than 4”x6” in size, or not one of the types of mesh listed in Inclusion Criteria #5.
7) Cannot tolerate general anesthesia.
8) Has any significant or unstable medical or psychiatric condition that, in the opinion of the Investigator, would interfere with his/her ability to participate in the study.
9) Is currently enrolled in another clinical study or undergoing treatment with another investigational drug or device.

2. Follow-up Schedule

All patients were scheduled to return for follow-up assessments post-surgery at Day 7 (±3 days); Day 14 (-3/+6 days); Month 1 (±7 days); Month 3 (±14 days); Month 6 (-21/ +14 days); Month 9 (-21/ +14 days); and Month 12 (-21/ +14 days).

Preoperatively, the patient’s medical history, demographic data, current analgesic usage, and hernia information was collected. Vital signs, subject pain (VAS) and Quality of Life assessment was also performed. All pre-surgical and surgical procedures up until mesh fixation and peritoneal closure (TAPP repairs only), were performed as per investigational site standard of care.

On the day of surgery, analgesic usage and vital signs were recorded. A pregnancy test was performed on women of child-bearing potential prior to surgery. Randomization to either Investigational or control device occurred at the surgery visit (Visit 2) and therefore the subjects were blinded to their randomly assigned treatment device prior to surgery and during the follow up period following surgery. Intraoperatively, hernia information (type and size) was confirmed as well as the use of investigational or control device and any inadvertent application, photograph of mesh fixation and peritoneal closure (where applicable) and an evaluation of any adverse events observed.

At discharge, pain medications, other pain management therapies and vital signs were recorded as well as any complications or adverse events. A pain (VAS) assessment of the hernia repair was also captured on discharge. Throughout follow-up, any suspected hernia recurrence was confirmed by ultrasound imaging. Postoperatively, the objective parameters measured during the study included:

- Analgesic usage or other pain management therapies at all post-operative follow-up visits.
- Vital signs (Day 14, Month 3, and Month 6).
- Clinician evaluation of hernia repair (Day 14 in-clinic visit, Month 3, and Month 6).
- Subject pain (Visual Analog Scale) assessment using VAS pain assessment tool at all post-operative follow-up visits.
- Subject Quality of Life (Carolina Comfort Scale) questionnaire at all post-operative follow- up visits.
- Adverse Event evaluation at all post-operative follow-up visits.

The schedule of assessments is summarized in Table 6 below.

Table 6: Schedule of assessments

	Pre-Surgery	Surgery	Discharge	Post-Surgery Visits							Unscheduled visit
Visit	1	2	3[3]	4	5	6	7	8	9	10	N/A
Day / Month	≤21 Days	Day 0	Day 0 or 1	Day 7	Day 14	Month 1	Month 3	Month 6	Month 9	Month 12	N/A
Visit Window (Days)				±3	-3 / +6	±7	±14	-21 / +14	-21 / +14	-21 / +14	N/A
Informed Consent	X										
Inclusion/ Exclusion	X										
Pregnancy Test (if applicable)		X[1]									
Medical History	X										
Analgesics usage	X	X[1]	X	X	X	X	X	X	X	X	X
Demographics	X										
Vital Signs (HR/BP/T/Ht/Wt)[4]	X	X[1]	X		X		X	X			X
Randomization[5]		X[2]									
Hernia Information (type & size)	X	X[2]									
Use of Investigational or control device		X[2]									
Number of Investigational or control device applications		X[2]									
Photograph following mesh fixation		X									
Photograph following peritoneal closure[6]		X									
Clinician evaluation of hernia repair & PE[7]					X		X	X			X
Subject Pain (0-10 VAS) Assessment	X		X	X	X	X	X	X	X	X	
Subject QOL Assessment	X			X	X	X	X	X	X	X	
AE Evaluation		X[2]	X	X	X	X	X	X	X	X	X

[1]Immediately prior to surgery
[2]During surgery
[3]At discharge post-surgery, either on same day as surgery or next day post-surgery according to standard of care.
[4]Height only required at Pre-surgery visit. Unless Pre-surgery (Visit 1), Surgery (Visit 2) and Discharge (Visit 3) occur on the same date, weight should be obtained for each separate visit. Vital signs may be obtained remotely at Month 3 and 6 visits as volunteered by subjects using their own devices as available (e.g. thermometer, weight scales, smart wearable technology).
[5]Patient must be blinded to the randomization device
[6]Photograph following peritoneal closure only required for TAPP repairs.
[7]Suspected hernia recurrence will be confirmed by ultrasound imaging following physical examination.
HR: Heart rate; BP: Blood pressure; T: Temperature; Ht :Height; Wt: Weight; PE: Physical Examination; VAS: Visual Analog Scale; QOL: Quality of Life; AE: Adverse Event.
Shaded columns are in-clinic visits.

3. Clinical Endpoints

With regards to success/failure criteria, the study was designed with a non-inferiority hypothesis for the primary effectiveness endpoint of pain at 6 months. Success was determined by improvement in pain not inferior to control device as measured by a VAS value (0 = no pain to 10 = most pain imaginable) from baseline (worst pain experienced within 1 month of screening visit) to six months post hernia repair.

The primary effectiveness endpoint was tested for non-inferiority of treatment to control with a predefined non-inferiority margin of 0.9 on the VAS scale. The primary effectiveness endpoint was assessed with the following hypothesis:

H_0: $\delta_T - \delta_C \geq 0.9$
H_a: $\delta_T - \delta_C < 0.9$

where δ is the change from baseline worst pain experienced within 1 month of screening visit) to 6-month on VAS for the appropriate treatment group.

With regard to effectiveness, there are six secondary endpoints in the clinical study, three of which have associated hypothesis tests.

• Recurrence rate in subjects following laparoscopic (TEP and TAPP) groin hernia repair by LIQUIFIX FIX8™ or control (AbsorbaTack™) at 6 months.

H0: $q_T - q_C \geq 10\%$
H1: $q_T - q_C < 10\%$,

where q is the recurrence rate at 6 months for the appropriate treatment group.

• Rate of successful hernia mesh fixation in subjects undergoing TEP and TAPP laparoscopic groin hernia repair.

H0: $p_C - p_T \geq 10\%$
H1: $p_C - p_T < 10\%$,

where p is the rate of successful hernia mesh fixation at time of surgery for the appropriate treatment group. Unsuccessful mesh fixation is defined as requiring the use of an alternative fixation device or additional procedure to achieve adequate fixation at time of surgery.

• Rate of successful peritoneal closure in subjects undergoing laparoscopic TAPP hernia repair.

H0: $\pi_C - \pi_T \geq 15\%$
H1: $\pi_C - \pi_T < 15\%$,

where π is the rate of peritoneal closure at time of surgery for the appropriate treatment group. Unsuccessful peritoneal closure is defined as requiring the use of an alternative fixation device or additional procedure to achieve adequate fixation at time of surgery. The participating Investigators in the control arm in the study were able to use AbsorbaTack™, sutures or staples for closure of the peritoneum.

With regards to safety, the following secondary endpoints were also evaluated during the study:

- Quality of life experienced by subjects following groin hernia repair by LIQUIFIX FIX8™ or control as measured by the Carolinas Comfort Scale (CCS) at baseline (prior to surgery), and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months, and 12 months following surgery.
- Pain experienced following laparoscopic (TEP and TAPP) groin hernia repair by LIQUIFIX FIX8™ or control device, as measured by VAS at discharge, and at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months following surgery.
- Safety of LIQUIFIX FIX8™ and control device for groin hernia repair by comparing incidence of adverse events in patients post-laparoscopic groin hernia repair.

B. Accountability of PMA Cohort

At the time of database lock, of 284 patients enrolled in the PMA study, 93% (266) patients are available for analysis at the completion of the study, the Month 12 post-operative visit.

In the ITT set analysis there was a total of 284 subjects included; 142 subjects were in the LIQUIFIX FIX8™ group and 142 subjects in the AbsorbaTack™ control group. In the PP set analysis, there was a total of 264 subjects: 131 subjects in the LIQUIFIX FIX8™ group and 133 subjects in the AbsorbaTack™ group. The accountability of all 284 ITT subjects enrolled in the study are presented in Table 7 below.

Table 7: Randomized Subject Follow-up Accountability

Group			Pre-surgery	Surgery	Discharge	1 Week	2 Weeks	1 Month	3 Months	6 Months	9 Months	12 Months
LIQUIFIX FIX8™ (N = 142)	Subject Follow-up	Eligible[1]	143	142	142	142	142	142	142	142	140	138
		Clinical Follow-up Performed	100.00 % (143 / 143)	100.00 % (142 / 142)	100.00 % (142 / 142)	97.89 % (139 / 142)	100.00 % (142 / 142)	97.18 % (138 / 142)	97.18 % (138 / 142)	95.77 % (136 / 142)	95.00 % (133 / 140)	95.65 % (132 / 138)
	Subject's Events Occurring Before Next Visit[2]	Subject Screen Failure During Surgery	1	0	0	0	0	0	0	0	0	0
		Subject Withdrew Consent	0	0	0	0	0	0	0	0	0	0
		Sponsor's Decision	0	0	0	0	0	0	0	0	0	0
		Investigator's Decision	0	0	0	0	0	0	0	0	0	0
		Subject experienced an SAE that prevented attending all study visits	0	0	0	0	0	0	0	0	0	1
		Subject Lost to Follow-up	0	0	0	0	0	0	0	1	2	6
		Other	0	0	0	0	0	0	0	0	0	0

Table 7: Randomized Subject Follow-up Accountability

Group			Pre-surgery	Surgery	Discharge	1 Week	2 Weeks	1 Month	3 Months	6 Months	9 Months	12 Months
AbsorbaTack™ (N = 142)	Subject Follow-up	Eligible[1]	142	142	142	142	141	141	141	140	139	138
		Clinical Follow-up Performed	100.00 % (142 / 142)	100.00 % (142 / 142)	100.00 % (142 / 142)	98.59 % (140 / 142)	100.00 % (141 / 141)	97.16 % (137 / 141)	90.78 % (128 / 141)	95.00 % (133 / 140)	94.24 % (131 / 139)	97.10 % (134 / 138)
	Subject's Events Occurring Before Next Visit[2]	Subject Screen Failure During Surgery	0	0	0	0	0	0	0	0	0	0
		Subject Withdrew Consent	0	0	0	1	0	0	0	0	0	0
		Sponsor's Decision	0	0	0	0	0	0	0	0	0	0
		Investigator's Decision	0	0	0	0	0	0	0	0	0	0
		Subject experienced an SAE that prevented attending all study visits	0	0	0	0	0	0	0	0	0	0
		Subject Lost to Follow-up	0	0	0	0	0	0	0	1	2	4
		Other	0	0	0	0	0	0	0	0	0	0

[1]Subjects are eligible if visit window opened prior to last follow-up date
[2]Exits assigned to visit column where study exit date precedes the visit window close date and is later than the previous visit win dow close date.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a hernia repair study performed in the US. Most subjects were White 249, 88.0%), male (270, 95.1%), and are more common with increasing age (mean: 58.94 ± 14.041), which is consistent with general hernia repair patient population. A total of 284 subjects were treated in a 1:1 ratio with 142 subjects treated to LIQUIFIX FIX8™ and 142 to control. Percentage comparisons between the control and treatment group showed no notable differences. When stratified by laparoscopic technique (TAPP/TEP), subjects were similar in age, gender, race and ethnicity, however, the Black or African American race was better represented in the

AbsorbaTack™ group treated by TAPP than by TEP technique 17.4% vs 0.0%). Subject demographics and baseline characteristics were well matched between arms.

Table 8: Demographics (ITT set)

	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack™ (N = 142)	All Subjects (N = 284)
Gender			
Female	7.0% (10 / 142)	2.8% (4 / 142)	4.9% (14 / 284)
Male	93.0% (132 / 142)	97.2% (138 / 142)	95.1% (270 / 284)
Age (years)			
n	142	142	284
Mean ± SD	59.41 ± 13.696	58.47 ± 14.411	58.94 ± 14.041
Median	61.00	59.00	60.00
Min, Max	22.0, 85.0	26.0, 89.0	22.0, 89.0
Race			
American Indian or Alaska Native	0.0% (0 / 142)	0.0% (0 / 141)	0.0% (0 / 283)
Asian	0.7% (1 / 142)	2.1% (3 / 141)	1.4% (4 / 283)
Black or African American	9.2% (13 / 142)	11.3% (16 / 141)	10.2% (29 / 283)
More than One Race	0.0% (0 / 142)	0.7% (1 / 141)	0.4% (1 / 283)
Native Hawaiian or Other Pacific Islander	0.0% (0 / 142)	0.0% (0 / 141)	0.0% (0 / 283)
White	90.1% (128 / 142)	85.8% (121 / 141)	88.0% (249 / 283)
Ethnicity			
Hispanic or Latino	2.8% (4 / 142)	2.8% (4 / 142)	2.8% (8 / 284)
Not Hispanic or Latino	97.2% (138 / 142)	97.2% (138 / 142)	97.2% (276 / 284)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the LIQUIFIX FIX8™ (treatment) cohort of 142 patients. The key safety outcomes for this study are presented below in Tables 12 to 16.

Adverse effects are reported in Tables 9 to 11.

Adverse effects that occurred in the PMA clinical study:

A total of 271 adverse events (AEs) have been reported in the clinical study across the two treatment arms. A clinical event committee (CEC) has partaken in the review and adjudication of all adverse events during the Study. The incidence of device-related AEs by subject were comparable in the treatment (34 subjects; 23.9%) and control (43 subjects; 30.3%) groups. Out of these, 18 patients (6 Treatment, 12 Control) had more than one possibly device related AE. In terms of Serious AEs (SAEs), the incidence of possibly device-related adverse events was comparable between the treatment and control groups with 5 events in 5 3.5% subjects of device related SAEs in the treatment group compared

to 4 events in 4 2.8%) subjects in the control group. No single patient had more than one possibly device-related serious AE.

Serious possibly device-related adverse events observed in the clinical study included neuralgia, hernia recurrence, mesh infection and intestinal obstruction. A summary of serious adverse events adjudicated by an independent Clinical Events Committee (CEC) as related to the device or procedure can be found in Table 10.1 below for the ITT population and Table 10.2 for the PP population. The percentage of Subjects with serious device and/or procedure related adverse events is similar across the ITT (6.7%) and PP (6.8%) population. There was a total 9 of possibly device related adverse events; 5 in the

Table 9: AEs - Device and/or Procedure Related (ITT set)

	LIQUIFIX FIX8™ (N = 142)		**AbsorbaTack™ (N = 142)**	
# Serious Adverse Events (ITT)	N=11		N=16	
Total related to study device[2]	3.5% (5/142)	5	2.8% (4/142)	4
Total related to study procedure[2]	6.3% (9/142)	9	7.0% (10/142)	10
# Adverse Events (ITT)	N= 114		N=157	
Total related to study device[2]	23.9% (34/142)	41	30.3% (43/142)	55
Total related to study procedure[2]	35.9% (51/142)	76	43.0% (61/142)	107
[2]Related includes possibly and definitely related.				

LIQUIFIX FIX8™ groups and 4 in the control tacker. The events in the LIQUIFIX FIX8™ group included two neuralgias, one recurrent hernia, one mesh infection and one small bowel obstruction. The control group possible device related adverse events included two hematoma which required further intervention, and two recurrent hernias. Specifically, the treatment group had two neuralgias which improved with time and on review of the clinical reporting form map of the site of application, the subject device was not applied on the nerves that were responsible for the neuralgias. In the single bowel obstruction, which occurred at an adhesion next to the cecum in an area where inadvertent device drop occurred, the study investigator could not conclusively attribute this adverse event to the subject device. Subsequent animal testing demonstrated that the subject device drops occurring outside the mesh area could be easily removed at any point after polymerization by peeling without incurring tissue damage. The tack control group experienced two hematomas and none were seen with the subject device. This was possibly device related and could be the result of the tissue penetrating mechanism of action associated with the control tacker.

Table 10.1: Serious AEs - Device and/or Procedure Related[1] (ITT)

	LIQUIFIX FIX8™ (N = 142)		AbsorbaTack™ (N = 142)		All Subjects (N = 284)	
Adverse Event Term[2]	**Number of Events**	**Number (%) of Subjects with Events**	**Number of Events**	**Number (%) of Subjects with Events**	**Number of Events**	**Number (%) of Subjects with Events**
Atrial fibrillation	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Hematoma	0	0 (0.0%)	2	2 (1.4%)	2	2 (0.7%)
Inguinal hernia	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Neuralgia	2	2 (1.4%)	0	0 (0.0%)	2	2 (0.7%)
Dizziness	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Hernia	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Incisional hernia	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Intestinal obstruction	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Medical device site infection	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%
Procedural pain	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Tooth abscess	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Urethral injury	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Urinary retention	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Urinary tract injury	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%
Vomiting	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Total	9	9 (6.3%)	10	10 (7.0%)	19	19 (6.7%)

[1]Related includes possibly and definitely related.
[2]Medical Dictionary for Regulatory Activities (MedDRA) Preferred Term

Device and/or procedure related serious adverse events for the PP population has been presented in Table 10.2 below.

Table 10.2: Serious AEs - Device and/or Procedure Related[1] (PP)

	LIQUIFIX FIX8™ (N = 131)		AbsorbaTack™ (N = 133)		All Subjects (N = 264)	
Adverse Event Term[2]	**Number of Events**	**Number (%) of Subjects with Events**	**Number of Events**	**Number (%) of Subjects with Events**	**Number of Events**	**Number (%) of Subjects with Events**
Hematoma	0	0 (0.0%)	2	2 (1.5%)	2	2 (0.8%)
Inguinal hernia	1	1 (0.8%	1	1 (0.8%)	2	2 (0.8%)
Neuralgia	2	2 (1.5%)	0	0 (0.0%)	2	2 (0.8%)
Atrial fibrillation	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Dizziness	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Hernia	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Incisional hernia	1	1 (0.8%)	0	0 (0.0%	1	1 (0.4%)
Intestinal obstruction	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)

Table 10.2: Serious AEs - Device and/or Procedure Related[1] (PP)

	LIQUIFIX FIX8™ (N = 131)		AbsorbaTack™ (N = 133)		All Subjects (N = 264)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Medical device site infection	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Procedural pain	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Tooth abscess	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Urethral injury	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Urinary retention	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Urinary tract injury	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Vomiting	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Total	9	9 (6.9%)	9	9 (6.8%)	18	18 (6.8%)

[1]Related includes possibly and definitely related.
[2]MedDRA Preferred Term

The majority of non-serious device and/or procedure related adverse events were seroma formation. Overall, there were 47 events related to seroma in 44 (15.5%) subjects. All cases were mild in severity, and none were considered only related to the device in both groups. Other notable frequent non-serious AEs were groin pain with 16 events 16 subjects; 5.6%) and urinary retention with 10 events 10; 3.5%). Possibly related non-serious AEs were comparable between groups with the following notable differences: the incidence of seroma 13.4% Treatment, 17.6% Control) and groin pain (2.8% Treatment, 8.5% Control) was lower in the treatment group. A summary of non- serious adverse events adjudicated by the CEC as possibly or definitely related to the device or procedure can be found in Table 11.1 below for the ITT population and Table 11.2 for the PP population. The percentage of Subjects with non-serious device and/or procedure related adverse events is similar across the ITT (36.3%) and PP (36.0%) population.

Table 11.1: Non-Serious AEs - Device and/or Procedure Related[1] (ITT)

	LIQUIFIX FIX8™ (N = 142)		AbsorbaTack™ (N = 142)		All Subjects (N = 284)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Seroma	20	19 13.4%	27	25 17.6%	47	44 15.5%
Groin pain	4	4 (2.8%)	12	12 (8.5%)	16	16 (5.6%)
Urinary retention	5	5 (3.5%)	5	5 (3.5%)	10	10 (3.5%)
Post procedural constipation	4	4 (2.8%)	3	3 (2.1%)	7	7 (2.5%)
Dysuria	2	2 (1.4%)	3	3 (2.1%)	5	5 (1.8%)
Hematoma	2	2 (1.4%)	3	3 (2.1%)	5	5 (1.8%)
Procedural nausea	0	0 (0.0%)	5	5 (3.5%)	5	5 (1.8%)

Table 11.1: Non-Serious AEs - Device and/or Procedure Related[1] (ITT)

	LIQUIFIX FIX8™ (N = 142)		AbsorbaTack™ (N = 142)		All Subjects (N = 284)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Testicular pain	3	3 (2.1%)	2	2 (1.4%)	5	5 (1.8%)
Musculoskeletal pain	4	4 (2.8%)	0	0 (0.0%)	4	4 (1.4%)
Pain	1	1 (0.7%)	3	2 (1.4%)	4	3 (1.1%)
Swelling	1	1 (0.7%)	3	2 (1.4%)	4	3 (1.1%)
Genital hemorrhage	2	2 (1.4%)	1	1 (0.7%)	3	3 (1.1%)
Cellulitis	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Hypoaesthesia	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Orchitis	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Post procedural hematuria	0	0 (0.0%)	2	2 (1.4%)	2	2 (0.7%)
Rash	0	0 (0.0%)	2	2 (1.4%)	2	2 (0.7%)
Spermatic cord inflammation	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Umbilical hernia	1	1 (0.7%)	1	1 (0.7%)	2	2 (0.7%)
Urinary retention postoperative	0	0 (0.0%)	2	2 (1.4%)	2	2 (0.7%)
Abdominal pain	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Abdominal pain lower	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Arthralgia	1	1 (0.7%)	0	0 (0.0%	1	1 (0.4%)
Back pain	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Burning sensation	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Change of bowel habit	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Constipation	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Dermatitis contact	1	1 (0.7%)	0	0 (0.0%	1	1 (0.4%)
Diarrhea	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Dyspepsia	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Flatulence	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Gastrointestinal procedural complication	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Incisional hernia	0	0 (0.0%	1	1 (0.7%)	1	1 (0.4%)
Inguinal mass	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Injection site hematoma	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Lymphadenitis	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Muscle strain	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Musculoskeletal chest pain	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Neuralgia	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Nodule	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Pollakiuria	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)

Table 11.1: Non-Serious AEs - Device and/or Procedure Related[1] (ITT)

	LIQUIFIX FIX8™ (N = 142)		AbsorbaTack™ (N = 142)		All Subjects (N = 284)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Postoperative wound infection	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%
Reflex test abnormal	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Scrotal hematoma	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Scrotal pain	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Testicular swelling	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Throat irritation	1	1 (0.7%)	0	0 (0.0%	1	1 (0.4%)
Urethral pain	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Urinary incontinence	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Urinary tract infection	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Urinary tract procedural complication	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Vomiting	1	1 (0.7%)	0	0 (0.0%)	1	1 (0.4%)
Wound dehiscence	0	0 (0.0%)	1	1 (0.7%)	1	1 (0.4%)
Total	67	46 32.4%	97	57 40.1%	164	103 (36.3%)

[1]Related includes possibly and definitely related.
[2]MedDRA Preferred Term

Table 11.2: Non-Serious AEs - Device and/or Procedure Related[1] (PP)

	LIQUIFIX FIX8™ (N = 131)		AbsorbaTack™ (N = 133)		All Subjects (N = 264)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Seroma	18	17 13.0%	26	24 18.0%	44	41 15.5%
Groin pain	4	4 (3.1%)	10	10 (7.5%)	14	14 (5.3%)
Urinary retention	5	5 (3.8%)	5	5 (3.8%)	10	10 (3.8%)
Post procedural constipation	4	4 (3.1%	3	3 (2.3%)	7	7 (2.7%)
Dysuria	2	2 (1.5%)	3	3 (2.3%)	5	5 (1.9%)
Procedural nausea	0	0 (0.0%)	5	5 (3.8%)	5	5 (1.9%)
Hematoma	1	1 (0.8%)	3	3 (2.3%)	4	4 (1.5%)
Musculoskeletal pain	4	4 (3.1%)	0	0 (0.0%)	4	4 (1.5%)
Pain	1	1 (0.8%)	3	2 (1.5%)	4	3 (1.1%
Testicular pain	3	3 (2.3%)	1	1 (0.8%)	4	4 (1.5%)
Genital hemorrhage	2	2 (1.5%)	1	1 (0.8%)	3	3 (1.1%)
Cellulitis	1	1 (0.8%)	1	1 (0.8%)	2	2 (0.8%)
Hypoaesthesia	1	1 (0.8%)	1	1 (0.8%)	2	2 (0.8%)

Table 11.2: Non-Serious AEs - Device and/or Procedure Related[1] (PP)

	LIQUIFIX FIX8™ (N = 131)		AbsorbaTack™ (N = 133)		All Subjects (N = 264)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Orchitis	1	1 (0.8%)	1	1 (0.8%)	2	2 (0.8%)
Post procedural haematuria	0	0 (0.0%)	2	2 (1.5%)	2	2 (0.8%)
Rash	0	0 (0.0%)	2	2 (1.5%)	2	2 (0.8%)
Spermatic cord inflammation	1	1 (0.8%)	1	1 (0.8%)	2	2 (0.8%)
Swelling	1	1 (0.8%)	1	1 (0.8%)	2	2 (0.8%)
Umbilical hernia	1	1 (0.8%)	1	1 (0.8%)	2	2 (0.8%
Urinary retention postoperative	0	0 (0.0%)	2	2 (1.5%)	2	2 (0.8%)
Abdominal pain	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Abdominal pain lower	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Arthralgia	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Back pain	0	0 (0.0%)	1	1 (0.8%	1	1 (0.4%)
Burning sensation	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Constipation	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Dermatitis contact	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Diarrhea	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Dyspepsia	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%
Flatulence	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Gastrointestinal procedural complication	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Incisional hernia	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Inguinal mass	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Injection site hematoma	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Lymphadenitis	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Muscle strain	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Musculoskeletal chest pain	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Neuralgia	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Nodule	0	0 (0.0%	1	1 (0.8%)	1	1 (0.4%)
Pollakiuria	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Postoperative wound infection	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Reflex test abnormal	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Scrotal hematoma	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Scrotal pain	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Testicular swelling	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Throat irritation	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)

Table 11.2: Non-Serious AEs - Device and/or Procedure Related[1] (PP)

	LIQUIFIX FIX8™ (N = 131)		AbsorbaTack™ (N = 133)		All Subjects (N = 264)	
Adverse Event Term[2]	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events	Number of Events	Number (%) of Subjects with Events
Urethral pain	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Urinary incontinence	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%
Urinary tract infection	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Urinary tract procedural complication	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Vomiting	1	1 (0.8%)	0	0 (0.0%)	1	1 (0.4%)
Wound dehiscence	0	0 (0.0%)	1	1 (0.8%)	1	1 (0.4%)
Total	64	43 32.8%	90	52 39.1%	154	95 36.0%

[1]Related includes possibly and definitely related.
[2]MedDRA Preferred Term

2. Effectiveness Results

Of the 284 patients randomized, the analysis of key (primary) effectiveness was based on 131/131 subjects in the LIQUIFIX FIX8™ treatment arm and 130/133 evaluable patients in the Control arm (in the PP completers dataset) and 269/284 patients (in the ITT completers dataset). The results are based on the 6-month follow-up completers for both the PP and ITT population. Primary effectiveness outcomes are presented in Table 12. Secondary effectiveness outcomes are presented in Table 13 to Table 15.

Primary Effectiveness: Change in VAS from baseline to 6 months post-hernia repair
Subjects were considered enrolled in the study once they were randomized. All randomized subjects are included in the intent-to-treat (ITT) population and analyzed according to the treatment to which they were randomized. Additional analyses were performed on the per-protocol (PP) population. The PP population included all subjects treated as randomized who do not have major protocol violations.

The mean change in VAS pain score as measured from 6 months compared to baseline (worst pain experienced within 1 month of screening visit) for LIQUIFIX FIX8™ was -4.9 ± 2.5 and the control was -5.1 ± 2.3 for both the PP and ITT population. Non-inferiority of LIQUIFIX FIX8™ versus AbsorbaTack™ was demonstrated since the upper limits of the two-sided 95% CI based on PP and ITT completers for the difference in the mean change in VAS pain score as measured from 6 months compared to baseline were less than the pre-defined non-inferiority margin set at 0.9.

The missing data rate for primary effectiveness endpoint was 1.14% 3 Subjects) for the PP population and 5.28% (15 Subjects) for the ITT population.

Table 12.1: Primary effectiveness endpoint: Change in VAS from baseline[1] to 6 months post hernia repair in subjects requiring laparoscopic TEP and TAPP hernia repair (PP set)

	LIQUIFIX FIX8™ (N = 131)	AbsorbaTack™ (N = 133)	Difference[2]	p-value[3]	Non-inferior (Yes/No)[4]
n Mean ± SD Median Min, Max	131 -4.9 ± 2.5 -4.7 -10.0, 2.0	130 -5.1 ± 2.3 -5.0 -10.0, -0.5			Yes
Least Squares Mean			0.22	0.011	
95% CI			-0.36, 0.80		

Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.

[1] Worst pain experienced within 1 month of screening visit

[2] LIQUIFIX FIX8™ - AbsorbaTack™

[3] One-sided p-value (Difference < 0.9), based on general linear model for treatment arm adjusted for laparoscopic repair technique with non-inferiority margin of 0.9

[4] Indicated by p-value < 0.025

Table 12.2: Primary efficacy endpoint: Change in VAS from baseline[1] to 6 months post hernia repair in subjects requiring laparoscopic TEP and TAPP hernia repair (ITT set)

	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack (N = 142)	Difference[2]	p-value[3]	Non-inferior (Yes/No)[4]
n Mean ± SD Median Min, Max	136 -4.9 ± 2.5 -4.5 -10.0, 2.0	133 -5.1 ± 2.3 -5.0 -10.0, -0.5			Yes
Least Squares Mean			0.25	0.013	
95% CI			-0.33, 0.82		

Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.

[1] Worst pain experienced within 1 month of screening visit

[2] LIQUIFIX FIX8™ - AbsorbaTack™

[3] One-sided p-value (Difference < 0.9), based on general linear model for treatment arm adjusted for laparoscopic repair technique with non-inferiority margin of 0.9

[4] Indicated by p-value < 0.025

Hypothesis Tested Secondary Effectiveness Endpoint Results

Hernia Recurrence at 6 months

A total of three (3) hernia recurrences were recorded in the clinical study; one for LIQUIFIX FIX8™ and two (2) for Control. Non-inferiority of LIQUIFIX FIX8™ versus AbsorbaTack™ was demonstrated since the upper limits of the two-sided 95% CI based on PP and ITT completers for the difference in hernia recurrence as measured from 6 months were less than the pre-defined non-inferiority margin set at 10%.

The missing data rate for secondary effectiveness endpoint hernia recurrence was 0.38% (1 Subject) for the PP population and 1.06% (3 Subjects) for the ITT population.

Table 13.1: Secondary effectiveness endpoint 1: Hernia Recurrence rate at 6 months in subjects following TEP and TAPP groin hernia repair (PP set)

	LIQUIFIX FIX8 (N = 131 Subjects)	AbsorbaTack (N = 133 Subjects)	Difference[1]	p-value[2]	Non-inferior (Yes/No)[3]
% (n/N	0.8% (1/131)	1.5% (2/132)	-0.8%	<0.001	Yes
95% CI	0.0%, 2.3%	0.0%, 3.6%	-3.3%, 1.8%		

*Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.*Note: Denominator includes subjects with hernia recurrence by visit or follow-up through the visit window open date.
[1] LIQUIFIX FIX8 - AbsorbaTack.
[2] Based on a Non-inferiority Farrington-Manning test with a 10% margin
[3] Indicated by Upper CI Limit < 10%

Table 13.2: Secondary Effectiveness Endpoint 1: Hernia recurrence rate at 6 months in subjects following TEP and TAPP groin hernia repair (ITT set)

	LIQUIFIX FIX8™ (N = 142 Subjects)	AbsorbaTack™ (N = 142 Subjects)	Difference[1]	p-value[2]	Non-inferior (Yes/No)[3]
% (n/N	0.7% (1/141)	1.4% (2/140)	-0.7%	<0.001	Yes
95% CI	0.0%, 2.1%	0.0%, 3.4%	-3.1%, 1.7%		

Note: Denominator includes subjects with hernia recurrence by visit or follow-up through the visit window open date
Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data..
[1] LIQUIFIX FIX8™ - AbsorbaTack™.
[2] Based on a Non-inferiority Farrington-Manning test with a 10% margin
[3] Indicated by Upper CI Limit < 10%

Recurrence rates up to 12-month follow-up have been presented in Table 13.3 below. There were no additional occurrences of recurrence after 6-month follow-up.

Table 13.3: Secondary endpoint: Hernia Recurrence rate[1] at 2 weeks, 3 months, 6 months, 9 months, and 12 months in subjects following TEP and TAPP groin hernia repair (ITT set)

Visit	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack™ (N = 142)
2 weeks	0.0% (0/142)	0.0% (0/141)
3 months	0.7% (1/142)	0.7% (1/141)
6 months	0.7% (1/141)	1.4% (2/140)
9 months	0.7% (1/139)	1.4% (2/138)
12 months	0.8% (1/133)	1.5% (2/135)

[1] Rates are cumulative. Subjects having hernia recurrence at earlier timepoints are carried forward to later dates. Denominator includes subjects with hernia recurrence by visit, confirmed visit attendance, and/or follow-up through the visit window open date.

Hernia Mesh Fixation at time of surgery

Both arms (treatment and control) achieved 100% successful mesh fixation at time of surgery. LIQUIFIX FIX8™ was considered non-inferior to Control device in both the ITT and PP completers at the Subject Level analysis.

Non-inferiority of LIQUIFIX FIX8™ versus AbsorbaTack™ was demonstrated since the lower limits of the two-sided 95% CI based on PP and ITT completers for the difference in hernia mesh fixation at time of surgery were greater than the pre-defined non-inferiority margin set at -10%. The missing data rate for secondary effectiveness endpoint hernia mesh fixation was 0% for both the PP population and ITT population.

Table 14.1: Secondary effectiveness endpoint 2: Rate of successful hernia mesh fixation in subjects undergoing TEP and TAPP laparoscopic groin hernia repair (PP set) Assessed Per-Subject

	LIQUIFIX FIX8™ (N = 180 Hernias N = 131 Subjects)	**AbsorbaTack™ (N = 193 Hernias N = 133 Subjects)**	**Difference[1]**	**p-value[2]**	**Non-inferior (Yes/No)[3]**
% (n/N	100.0% (131/131)	100.0% (133/133)	-0.0%	<0.001	Yes
95% CI	100.0%, 100.0%	100.0%, 100.0%	-0.1%, 0.1%		

Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.

[1] LIQUIFIX FIX8™ - AbsorbaTack™.

[2] Based on a Non-inferiority Farrington-Manning test with a 10% margin. 0.001 added to zero-cells to calculate CI and p-value.

[3] Indicated by Lower CI Limit > -10%

Table 14.2: Secondary effectiveness endpoint 2: Rate of successful hernia mesh fixation in subjects undergoing TEP and TAPP laparoscopic groin hernia repair (ITT set) Assessed Per-Subject

	LIQUIFIX FIX8™ (N = 195 Hernias N = 142 Subjects)	**AbsorbaTack™ (N = 204 Hernias N = 142 Subjects)**	**Difference[1]**	**p-value[2]**	**Non-inferior (Yes/No)[3]**
% (n/N	100.0% (142/142)	100.0% (142/142)	0.0%	<0.001	Yes
95% CI	100.0%, 100.0%	100.0%, 100.0%	-0.1%, 0.1%		

Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.

[1] LIQUIFIX FIX8™ - AbsorbaTack™.

[2] Based on a Non-inferiority Farrington-Manning test with a 10% margin. 0.001 added to zero-cells to calculate CI and p-value.

[3] Indicated by Lower CI Limit > -10%

Peritoneal Closure at time of surgery (TAPP repairs only)

LIQUIFIX FIX8™ achieved an 88.4% peritoneal closure success rate in comparison to the Control arm's 90.5% when assessed at the Subject Level. Non-inferiority of LIQUIFIX FIX8™ versus AbsorbaTack™ was demonstrated since the lower limits of the two-sided 95% CI based on PP and ITT completers for the difference in peritoneal closure at time of surgery were greater than the pre-defined non-inferiority margin set at -15%.

The missing data rate for secondary effectiveness endpoint peritoneal closure at time of surgery was 0% for both the PP and ITT population.

Table 15.1: Secondary effectiveness endpoint 3: Rate of successful peritoneal closure in subjects undergoing laparoscopic TAPP hernia repair (PP set) Assessed Per-Subject

	LIQUIFIX FIX8™ (N = 108 Hernias N = 86 Subjects)	AbsorbaTack™ (N = 112 Hernias N = 84 Subjects)	Difference[1]	p-value[2]	Non-inferior (Yes/No)[3]
% (n/N)	88.4% (76/86)	90.5% (76/84)	-2.1%	0.006	Yes
95% CI	81.6%, 95.1%	84.2%, 96.8%	-11.4%, 7.1%		

Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.
[1] LIQUIFIX FIX8™- AbsorbaTack™.
[2] Based on a Non-inferiority Farrington-Manning test with a 15% margin
[3] Indicated by Lower CI Limit > -15%

Table 15.2: Secondary effectiveness endpoint 3: Rate of successful peritoneal closure in subjects undergoing laparoscopic TAPP hernia repair (ITT set) Assessed Per-Subject

	LIQUIFIX FIX8™ (N = 117 Hernias N = 94 Subjects)	AbsorbaTack™ (N = 122 Hernias N = 92 Subjects)	Difference[1]	p-value[2]	Non-inferior (Yes/No)[3]
% (n/N	87.2% (82/94)	91.3% (84/92)	-4.1%	0.012	Yes
95% CI	80.5%, 94.0%	85.5%, 97.1%	-13.0%, 4.8%		

Note: The denominator is the number of evaluable data points and may be less than the analysis population size due to missing data.
[1] LIQUIFIX FIX8™- AbsorbaTack™.
[2] Based on a Non-inferiority Farrington-Manning test with a 15% margin
[3] Indicated by Lower CI Limit > -15%

Ancillary Secondary Effectiveness Endpoint Results

Quality of Life (Carolina Comfort Scale)

Quality of Life (QOL) was assessed at each post-operative follow-up visit using a Carolina Comfort Scale questionnaire which assessed pain, sensation of mesh and movement limitations over various activities. A scale of 0 (No symptoms) to 5 (Disabling symptoms) is used to record subject Quality of Life. The accumulative total score can range from 0 to 115 with the higher the score the lower the health-related quality of life. Numerical improvement was observed for comparison of QOL at 12-month post-operative versus 1-week post-surgery, with a mean change of -15.6 ± 16.0 for LIQUIFIX FIX8™ and -15.3 ± 16.1 for control.

Table 16: Secondary endpoint: Carolinas Comfort Scale (CCS) Questionnaire Total Score at 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months and 12 months (ITT set)

	LIQUIFIX FIX8 (N = 142)		AbsorbaTack (N = 142)	
	Total Score **n** **Mean ± SD** **Median (p25, p75)** **Min, Max**	**Change from 1 week** **n** **Mean ± SD** **Median (p25, p75)** **Min, Max**	**Total Score** **n** **Mean ± SD** **Median (p25, p75)** **Min, Max**	**Change from 1 week** **n** **Mean ± SD** **Median (p25, p75)** **Min, Max**
1 week	129 16.1 ± 15.7 12.0 (5.0, 22.0) 0.0, 83.0	N/A	129 16.9 ± 16.6 13.0 (5.0, 24.0) 0.0, 80.0	N/A
2 weeks	136 8.6 ± 13.2 3.0 (0.0, 11.5) 0.0, 64.0	126 -7.7 ± 12.4 -5.0 (-13.0, 0.0) -55.0, 26.0	137 10.2 ± 15.2 4.0 (1.0, 12.0) 0.0, 77.0	128 -7.0 ± 13.2 -5.0 (-11.0, -1.0) -61.0, 47.0
1 month	136 4.8 ± 8.2 2.0 (0.0, 6.0) 0.0, 53.0	125 -12.4 ± 12.6 -9.0 (-18.0, -3.0) -55.0, 12.0	134 5.2 ± 10.5 1.0 (0.0, 5.0) 0.0, 82.0	124 -12.2 ± 14.6 -9.0 (-17.5, -3.0) -75.0, 41.0
3 months	137 2.0 ± 7.6 0.0 (0.0, 1.0) 0.0, 75.0	124 -14.6 ± 16.9 -11.0 (-20.5, -4.0) -83.0, 47.0	126 2.7 ± 8.5 0.0 (0.0, 2.0) 0.0, 69.0	117 -14.4 ± 15.9 -10.0 (-21.0, -3.0) -79.0, 28.0
6 months	136 1.2 ± 3.8 0.0 (0.0, 0.0) 0.0, 24.0	123 -15.1 ± 16.0 -12.0 (-22.0, -3.0) -83.0, 15.0	133 1.8 ± 4.4 0.0 (0.0, 1.0) 0.0, 35.0	122 -15.3 ± 16.7 -11.0 (-23.0, -4.0) -80.0, 24.0
9 months	133 0.9 ± 3.1 0.0 (0.0, 0.0) 0.0, 29.0	123 -15.6 ± 16.3 -12.0 (-24.0, -4.0) -83.0, 24.0	130 1.4 ± 3.8 0.0 (0.0, 1.0) 0.0, 27.0	120 -15.7 ± 16.5 -11.0 (-22.0, -4.5) -80.0, 14.0
12 months	131 0.5 ± 1.5 0.0 (0.0, 0.0) 0.0, 11.0	120 -15.6 ± 16.0 -11.0 (-23.0, -4.5) -83.0, 6.0	133 0.8 ± 3.5 0.0 (0.0, 0.0) 0.0, 34.0	122 -15.3 ± 16.1 -11.0 (-22.0, -4.0) -80.0, 23.0

If more than 2 patient responses within a domain were missing, then the summary score is set to missing. Otherwise mean imputation is used for missing responses.
Score unable to be calculated prior to surgery because patient has not had hernia repair.

Pain (VAS)

Pain was assessed at each post-operative follow-up visit using a VAS scale tool. The results of the primary effectiveness endpoint of change in VAS pain at 6-month from baseline is described above. Numerical reduction was observed in the results from the 12-month follow-up period, with LIQUIFIX FIX8™ mean change of -3.6 ± 2.9 (N=132) and Control -3.5 ± 3.1 (N=133) for the ITT completers.

Table 17: Secondary endpoint: VAS at pre-surgery, discharge, 1 week, 2 weeks, 1 month, 3 months, 6 months, 9 months, and 12 months (ITT set)

	LIQUIFIX FIX8™ (N = 142)		AbsorbaTack™ (N = 142)	
	VAS n Mean ± SD Median (p25, p75) Min, Max	VAS Change from Pre-Surgery n Mean ± SD Median (p25, p75) Min, Max	VAS n Mean ± SD Median (p25, p75) Min, Max	VAS Change from Pre-Surgery n Mean ± SD Median (p25, p75) Min, Max
Pre-surgery	142 3.8 ± 2.9 3.3 (1.5, 6.0) 0.0, 10.0	N/A	142 3.8 ± 3.0 3.0 (1.0, 6.5) 0.0, 10.0	N/A
Discharge	142 3.5 ± 2.1 3.5 (2.0, 5.0) 0.0, 10.0	142 -0.3 ± 3.4 0.0 (-3.0, 2.0) -8.2, 6.5	142 3.7 ± 1.9 4.0 (2.0, 5.0) 0.0, 10.0	142 -0.1 ± 3.5 0.0 (-3.0, 2.9) -8.0, 7.0
1 week	139 2.3 ± 1.9 2.0 (1.0, 3.5) 0.0, 9.0	139 -1.5 ± 2.8 -1.0 (-3.9, 0.5) -10.0, 4.0	140 2.3 ± 1.9 2.0 (1.0, 3.5) 0.0, 7.0	140 -1.5 ± 3.1 -1.0 (-3.3, 1.0) -10.0, 7.0
2 weeks	141 1.0 ± 1.4 0.5 (0.0, 1.5) 0.0, 8.0	141 -2.8 ± 2.8 -2.0 (-4.9, -0.9) -10.0, 2.1	141 1.1 ± 1.3 1.0 (0.0, 2.0) 0.0, 6.0	141 -2.7 ± 2.9 -2.0 (-5.0, -0.5) -9.5, 4.0
1 month	138 0.6 ± 1.0 0.0 (0.0, 1.0) 0.0, 5.0	138 -3.2 ± 2.8 -2.8 (-5.1, -0.9) -10.0, 1.0	137 0.7 ± 1.2 0.0 (0.0, 1.0) 0.0, 7.0	137 -3.1 ± 3.1 -2.5 (-5.5, -1.0) -10.0, 6.5
3 months	138 0.2 ± 0.7 0.0 (0.0, 0.0) 0.0, 5.2	138 -3.6 ± 2.9 -3.0 (-6.0, -1.0) -10.0, 1.0	129 0.4 ± 0.9 0.0 (0.0, 0.0) 0.0, 7.0	129 -3.4 ± 3.1 -2.1 (-6.0, -1.0) -10.0, 3.0
6 months	136 0.2 ± 0.8 0.0 (0.0, 0.0) 0.0, 6.0	136 -3.6 ± 3.0 -3.0 (-6.0, -1.0) -10.0, 3.0	133 0.3 ± 0.7 0.0 (0.0, 0.0) 0.0, 4.0	133 -3.5 ± 3.1 -3.0 (-6.0, -1.0) -10.0, 2.0
9 months	133 0.1 ± 0.3 0.0 (0.0, 0.0) 0.0, 2.0	133 -3.7 ± 2.9 -3.0 (-6.0, -1.4) -10.0, 1.0	131 0.2 ± 0.6 0.0 (0.0, 0.0) 0.0, 3.5	131 -3.5 ± 3.0 -3.0 (-6.0, -1.0) -10.0, 1.0
12 months	132 0.1 ± 0.4 0.0 (0.0, 0.0) 0.0, 3.0	132 -3.6 ± 2.9 -3.0 (-6.0, -1.0) -10.0, 0.0	133 0.1 ± 0.6 0.0 (0.0, 0.0) 0.0, 6.0	133 -3.5 ± 3.1 -3.0 (-6.0, -1.0) -10.0, 6.0

3. Subgroup Analyses

The following pre-operative characteristics were evaluated for potential association with outcomes: Size of hernia (<3cm or ≥3cm), Sex of subject (M or F), Age of subject (in years – Dichotomized at Median Age, Femoral or Inguinal groin hernia, Direct or indirect groin hernia, Primary or recurrent groin hernia, Unilateral or bilateral groin hernia, TEP or TAPP hernia repair procedure, Multifocal or Single hernia, Comparison of 6 month visit assessments obtained either in-clinic or obtained remotely and Concomitant or No Concomitant Hernia Repair. Difference between randomized groups in change in VAS from baseline to 6-months post hernia repair (primary endpoint) within each subgroup was analyzed and the results were presented for both the PP (Table 18) and ITT (Table 19) completers. Overall, subjects in the control group show larger change in VAS from baseline to 6-months. Specifically, compared to the treatment group, at least 0.5 more reduction in change in VAS from baseline to 6-months post hernia repair in the control group was observed in patients with TEP laparoscopic technique, patients with hernia size ≥ 3 cm, or patients with direct hernia for both PP and ITT completers.

Table 18: Subgroup analyses of Primary Endpoint - Change in VAS from baseline[1] to six months post hernia repair: summary statistics (PP set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 131)	AbsorbaTack™ (N = 133)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
Sex of Subject					**0.187**
Female	n Mean ± SD Median Min, Max	9 -4.6 ± 3.0 -5.0 -9.0, 0.0	3 -6.8 ± 2.0 -8.0 -8.0, -4.5		
	Least Squares Mean			2.31	
	95% CI			-0.83, 5.45	
Male	n Mean ± SD Median Min, Max	122 -4.9 ± 2.5 -4.6 -10.0, 2.0	127 -5.1 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.16	
	95% CI			-0.43, 0.76	
Age					**0.985**
< 61	n Mean ± SD Median Min, Max	57 -5.1 ± 2.7 -4.5 -10.0, 2.0	71 -5.2 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.19	
	95% CI			-0.65, 1.03	
≥ 61	n Mean ± SD Median Min, Max	74 -4.8 ± 2.4 -5.0 -9.0, 0.0	59 -5.0 ± 2.3 -4.9 -10.0, -0.5		
	Least Squares Mean			0.18	
	95% CI			-0.64, 1.01	
Laparoscopic Technique					**0.385**
TAPP	n Mean ± SD Median Min, Max	86 -5.2 ± 2.3 -5.0 -10.0, 0.0	81 -5.2 ± 2.5 -5.0 -10.0, -0.5		
	Least Squares Mean			0.03	
	95% CI			-0.70, 0.76	
TEP	n Mean ± SD Median Min, Max	45 -4.3 ± 2.8 -4.0 -10.0, 2.0	49 -4.9 ± 1.9 -4.9 -10.0, -1.0		
	Least Squares Mean			0.56	
	95% CI			-0.41, 1.54	
Bilateral or Unilateral Hernia					**0.802**

Table 18: Subgroup analyses of Primary Endpoint - Change in VAS from baseline[1] to six months post hernia repair: summary statistics (PP set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 131)	AbsorbaTack™ (N = 133)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
Bilateral	n Mean ± SD Median Min, Max	49 -4.4 ± 2.4 -4.0 -9.0, 2.0	60 -4.8 ± 2.3 -4.5 -10.0, -0.5		
	Least Squares Mean			0.35	
	95% CI			-0.56, 1.25	
Unilateral	n Mean ± SD Median Min, Max	82 -5.2 ± 2.5 -5.0 -10.0, 0.0	70 -5.3 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.20	
	95% CI			-0.57, 0.96	
Multifocal Hernia[3]					**0.716**
No	n Mean ± SD Median Min, Max	113 -4.9 ± 2.5 -4.7 -10.0, 2.0	107 -5.1 ± 2.2 -5.0 -10.0, -0.5		
	Least Squares Mean			0.18	
	95% CI			-0.46, 0.82	
Yes	n Mean ± SD Median Min, Max	18 -4.6 ± 2.3 -4.5 -9.0, -0.5	23 -5.0 ± 2.7 -5.0 -10.0, -0.5		
	Least Squares Mean			0.48	
	95% CI			-1.01, 1.97	
Hernia Size[3]					**0.179**
<3cm	n Mean ± SD Median Min, Max	57 -5.2 ± 2.5 -5.0 -10.0, 2.0	58 -5.0 ± 2.2 -5.0 -9.3, -0.5		
	Least Squares Mean			-0.23	
	95% CI			-1.11, 0.65	
≥3cm	n Mean ± SD Median Min, Max	74 -4.6 ± 2.5 -4.5 -10.0, 0.0	72 -5.2 ± 2.4 -5.0 -10.0, -0.5		
	Least Squares Mean			0.57	
	95% CI			-0.21, 1.35	
Direct or Indirect Hernia[3]					**0.070**

Table 18: Subgroup analyses of Primary Endpoint - Change in VAS from baseline[1] to six months post hernia repair: summary statistics (PP set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 131)	AbsorbaTack™ (N = 133)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
Direct	n Mean ± SD Median Min, Max	43 -4.2 ± 2.3 -4.0 -10.0, -0.5	49 -5.1 ± 2.6 -4.5 -10.0, -1.0		
	Least Squares Mean			0.89	
	95% CI			-0.09, 1.87	
Indirect	n Mean ± SD Median Min, Max	84 -5.3 ± 2.6 -5.0 -10.0, 2.0	74 -5.0 ± 2.1 -5.0 -10.0, -0.5		
	Least Squares Mean			-0.26	
	95% CI			-1.01, 0.50	
Primary or Recurrent Hernia[3]					**0.985**
Primary	n Mean ± SD Median Min, Max	113 -4.9 ± 2.5 -4.7 -10.0, 2.0	113 -5.1 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.25	
	95% CI			-0.38, 0.87	
Recurrent	n Mean ± SD Median Min, Max	15 -4.7 ± 2.3 -4.5 -9.0, -2.0	15 -5.1 ± 2.2 -4.0 -10.0, -3.0		
	Least Squares Mean			0.26	
	95% CI			-1.46, 1.99	
Femoral or Inguinal Hernia[3]					**0.680**
Femoral	n Mean ± SD Median Min, Max	2 -4.0 ± 2.8 -4.0 -6.0, -2.0	1 -3.0 ± 0.0 -3.0 -3.0, -3.0		
	Least Squares Mean			-1.00	
	95% CI			-6.78, 4.78	
Inguinal	n Mean ± SD Median Min, Max	127 -4.9 ± 2.5 -4.7 -10.0, 2.0	129 -5.1 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.22	
	95% CI			-0.37, 0.81	
In-clinic or Remote Visit					**0.712**

Table 18: Subgroup analyses of Primary Endpoint - Change in VAS from baseline[1] to six months post hernia repair: summary statistics (PP set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 131)	AbsorbaTack™ (N = 133)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
In-clinic	n Mean ± SD Median Min, Max	71 -4.9 ± 2.6 -5.0 -10.0, 2.0	73 -5.2 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.32	
	95% CI			-0.47, 1.11	
Remote	n Mean ± SD Median Min, Max	60 -4.9 ± 2.4 -4.5 -10.0, 0.0	57 -5.0 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.10	
	95% CI			-0.78, 0.97	
Concomitant Hernia Repair					**0.632**
No	n Mean ± SD Median Min, Max	115 -4.9 ± 2.4 -5.0 -10.0, 0.0	103 -5.1 ± 2.4 -5.0 -10.0, -0.5		
	Least Squares Mean			0.17	
	95% CI			-0.48, 0.81	
Yes	n Mean ± SD Median Min, Max	16 -4.6 ± 3.2 -4.4 -9.0, 2.0	27 -5.1 ± 2.0 -4.9 -10.0, -1.8		
	Least Squares Mean			0.56	
	95% CI			-0.93, 2.05	

[1] Worst pain experienced within 1 month of screening visit

[2] LIQUIFIX FIX8™ - AbsorbaTack™. Based on general linear model adjusted for laparoscopic repair technique (with exception of laparoscopic technique subgroup)

[3] Hernia level subgroup. Subjects categorized by characteristics of largest hernia observed. Hernia size was captured as at least or less than 3cm. If no differences, then mesh size was used to identify larger hernia. If no differences in mesh size and subgroup characteristics differed across hernias, the subject was excluded from the specific subgroup analysis.

Subgroup analysis was also performed for the ITT completers, taking into account bilateral hernias with differing characteristics as independent observations (see footnote 3), in Table 19 below, showing similar results.

Table 19: Subgroup analyses of Primary Endpoint – Change in VAS from baseline[1] to six months post hernia repair: summary statistics (ITT set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack™ (N = 142)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
Sex of Subject					**0.134**
Female	n Mean ± SD Median Min, Max	10 -4.5 ± 2.9 -4.5 -9.0, 0.0	4 -6.9 ± 1.7 -7.5 -8.0, -4.5		
	Least Squares Mean			2.35	
	95% CI			-0.45, 5.14	
Male	n Mean ± SD Median Min, Max	126 -4.9 ± 2.5 -4.5 -10.0, 2.0	129 -5.0 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.17	
	95% CI			-0.42, 0.76	
Age					**0.933**
< 61	n Mean ± SD Median Min, Max	60 -5.1 ± 2.7 -4.5 -10.0, 2.0	73 -5.3 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.23	
	95% CI			-0.59, 1.06	
≥ 61	n Mean ± SD Median Min, Max	76 -4.7 ± 2.3 -5.0 -9.0, 0.0	60 -4.9 ± 2.3 -4.7 -10.0, -0.5		
	Least Squares Mean			0.18	
	95% CI			-0.63, 1.00	
Laparoscopic Technique					**0.493**
TAPP	n Mean ± SD Median Min, Max	89 -5.1 ± 2.3 -5.0 -10.0, 0.0	83 -5.2 ± 2.5 -5.0 -10.0, -0.5		
	Least Squares Mean			0.10	
	95% CI			-0.63, 0.82	
TEP	n Mean ± SD Median Min, Max	47 -4.4 ± 2.8 -4.0 -10.0, 2.0	50 -4.9 ± 1.9 -5.0 -10.0, -1.0		
	Least Squares Mean			0.51	
	95% CI			-0.45, 1.47	
Bilateral or Unilateral Hernia					**0.862**

Table 19: Subgroup analyses of Primary Endpoint – Change in VAS from baseline[1] to six months post hernia repair: summary statistics (ITT set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack™ (N = 142)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
Bilateral	n Mean ± SD Median Min, Max	51 -4.5 ± 2.4 -4.0 -9.0, 2.0	61 -4.8 ± 2.3 -4.5 -10.0, -0.5		
	Least Squares Mean			0.22	
	95% CI			-0.67, 1.12	
Unilateral	n Mean ± SD Median Min, Max	85 -5.1 ± 2.5 -5.0 -10.0, 0.0	72 -5.4 ± 2.2 -5.1 -10.0, -0.5		
	Least Squares Mean			0.33	
	95% CI			-0.43, 1.08	
Multifocal Hernia[3]					**0.868**
No	n Mean ± SD Median Min, Max	122 -4.9 ± 2.5 -4.6 -10.0, 2.0	115 -5.1 ± 2.2 -5.0 -10.0, -0.5		
	Least Squares Mean			0.17	
	95% CI			-0.44, 0.78	
Yes	n Mean ± SD Median Min, Max	19 -4.8 ± 2.4 -5.0 -9.0, -0.5	24 -5.1 ± 2.7 -5.0 -10.0, -0.5		
	Least Squares Mean			0.30	
	95% CI			-1.15, 1.75	
Hernia Size[3]					**0.258**
<3cm	n Mean ± SD Median Min, Max	74 -5.1 ± 2.5 -4.9 -10.0, 2.0	81 -4.9 ± 2.2 -4.5 -10.0, -0.5		
	Least Squares Mean			-0.11	
	95% CI			-0.86, 0.65	
≥3cm	n Mean ± SD Median Min, Max	76 -4.7 ± 2.5 -4.5 -10.0, 0.0	72 -5.2 ± 2.4 -5.0 -10.0, -0.5		
	Least Squares Mean			0.51	
	95% CI			-0.26, 1.28	
Direct or Indirect Hernia[3]					**0.147**

Table 19: Subgroup analyses of Primary Endpoint – Change in VAS from baseline[1] to six months post hernia repair: summary statistics (ITT set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack™ (N = 142)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
Direct	n Mean ± SD Median Min, Max	52 -4.2 ± 2.5 -4.0 -10.0, 2.0	65 -5.1 ± 2.5 -4.9 -10.0, -1.0		
	Least Squares Mean			0.89	
	95% CI			0.02, 1.76	
Indirect	n Mean ± SD Median Min, Max	96 -5.1 ± 2.5 -5.0 -10.0, 2.0	85 -5.1 ± 2.1 -5.0 -10.0, -0.5		
	Least Squares Mean			0.06	
	95% CI			-0.64, 0.76	
Primary or Recurrent Hernia[3]					**0.684**
Primary	n Mean ± SD Median Min, Max	120 -4.8 ± 2.5 -4.5 -10.0, 2.0	119 -5.1 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.33	
	95% CI			-0.28, 0.95	
Recurrent	n Mean ± SD Median Min, Max	21 -5.1 ± 2.4 -5.0 -9.0, -2.0	20 -5.2 ± 2.3 -4.3 -10.0, -2.0		
	Least Squares Mean			-0.00	
	95% CI			-1.50, 1.49	
Femoral or Inguinal Hernia[3]					**0.547**
Femoral	n Mean ± SD Median Min, Max	4 -4.3 ± 2.6 -4.0 -7.0, -2.0	1 -3.0 ± . -3.0 -3.0, -3.0		
	Least Squares Mean			-1.38	
	95% CI			-6.66, 3.89	
Inguinal	n Mean ± SD Median Min, Max	135 -4.9 ± 2.5 -4.5 -10.0, 2.0	132 -5.1 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.24	
	95% CI			-0.33, 0.82	
In-clinic or Remote Visit					**0.762**

Table 19: Subgroup analyses of Primary Endpoint – Change in VAS from baseline[1] to six months post hernia repair: summary statistics (ITT set)

Subgroup	Subgroup	LIQUIFIX FIX8™ (N = 142)	AbsorbaTack™ (N = 142)	Difference[2]	Type III Interaction p-value (Subgroup Treatment Arm)
In-clinic	n Mean ± SD Median Min, Max	75 -4.9 ± 2.6 -5.0 -10.0, 2.0	76 -5.2 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.32	
	95% CI			-0.45, 1.09	
Remote	n Mean ± SD Median Min, Max	61 -4.9 ± 2.4 -4.5 -10.0, 0.0	57 -5.0 ± 2.3 -5.0 -10.0, -0.5		
	Least Squares Mean			0.14	
	95% CI			-0.73, 1.02	
Concomitant Hernia Repair					**0.666**
No	n Mean ± SD Median Min, Max	120 -4.9 ± 2.4 -4.5 -10.0, 0.0	106 -5.1 ± 2.4 -5.0 -10.0, -0.5		
	Least Squares Mean			0.20	
	95% CI			-0.43, 0.83	
Yes	n Mean ± SD Median Min, Max	16 -4.6 ± 3.2 -4.4 -9.0, 2.0	27 -5.1 ± 2.0 -4.9 -10.0, -1.8		
	Least Squares Mean			0.56	
	95% CI			-0.94, 2.05	

[1] Worst pain experienced within 1 month of screening visit
[2] LIQUIFIX FIX8™ - AbsorbaTack™. Based on general linear model adjusted for laparoscopic repair technique (with exception of laparoscopic technique subgroup)
[3] Hernia level subgroup. Subjects categorized by characteristics of all hernias observed. Bilateral subjects with differing hernia characteristics between hernias are included twice, represented uniquely within each subgroup category. For example, a bilateral subject with left side primary hernia and right side recurrent hernia is included in both subgroup categories.

Poolability

Table 20.1 and Table 21.1 shows the primary endpoint results (6 Month Pain VAS change from baseline) for each treatment group at each site for the ITT completers and PP completers, respectively. It was noted that all Site 03 procedures were performed with TAPP (40/40 ITT), whereas 97% of Site 04 procedures were TEP (31/32 ITT).

Table 20.1: Site Poolability: Change in VAS from baseline[1] to six months post hernia repair by site (PP set)

Site	LIQUIFIX FIX8 (N = 131)	AbsorbaTack (N = 133)
Site 1		
n	21	20
Mean ± SD	-5.0 ± 2.7	-4.9 ± 1.8
Median (p25, p75)	-5.6 (-6.5, -3.5)	-5.0 (-6.3, -3.4)
Min, Max	-8.0, 2.0	-8.0, -1.8
Site 2		
n	28	24
Mean ± SD	-4.9 ± 2.6	-5.1 ± 2.1
Median (p25, p75)	-4.3 (-7.3, -3.0)	-5.0 (-6.8, -3.0)
Min, Max	-10.0, 0.0	-10.0, -2.0
Site 3		
n	16	17
Mean ± SD	-4.4 ± 2.9	-3.0 ± 1.5
Median (p25, p75)	-4.0 (-5.5, -2.5)	-3.0 (-4.0, -2.0)
Min, Max	-10.0, 0.0	-6.0, -0.5
Site 4		
n	15	16
Mean ± SD	-3.4 ± 1.3	-4.8 ± 1.9
Median (p25, p75)	-3.0 (-4.1, -2.0)	-4.5 (-6.0, -4.0)
Min, Max	-6.5, -2.0	-10.0, -2.0
Site 5		
n	51	53
Mean ± SD	-5.4 ± 2.4	-6.0 ± 2.4
Median (p25, p75)	-5.5 (-8.0, -4.0)	-6.0 (-8.0, -4.0)
Min, Max	-10.0, -0.5	-10.0, -1.0

[1]Worst pain experienced within 1 month of screening visit

Table 20.2: Site Poolability: Change in VAS from baseline1 to six months post hernia repair: regression model results (PP set)

Covariate	Parameter Estimate (95% CI)	p-value[2]
Intercept	-5.41 (-6.28, -4.55)	
Site 1	0.68 (-0.58, 1.95)	0.0001
Site 2	0.91 (-0.19, 2.02)	
Site 3	3.17 (1.90, 4.44)	
Site 4	0.59 (-0.83, 2.02)	
Site 5	Reference	
Treatment (Ref=Control)	0.56 (-0.32, 1.45)	0.6933
Site 1*Treatment Arm	-0.64 (-2.30, 1.03)	0.1108
Site 2*Treatment Arm	-0.40 (-1.93, 1.14)	
Site 3*Treatment Arm	-2.05 (-3.85, -0.25)	
Site 4*Treatment Arm	0.89 (-0.96, 2.74)	
Site 5*Treatment Arm	Reference	

Covariate	Parameter Estimate (95% CI)	p-value[2]
Repair Technique: TAPP (Ref=TEP)	-0.71 (-1.49, 0.07)	0.0741

[1]Worst pain experienced within 1 month of screening visit
[2]Type III

Table 21.1: Site Poolability: Change in VAS from baseline[1] to six months post hernia repair by site (ITT set)

Site	LIQUIFIX FIX8 (N = 142)	AbsorbaTack (N = 142)
Site 1		
n	22	21
Mean ± SD	-5.2 ± 2.7	-5.0 ± 1.8
Median (p25, p75)	-5.8 (-7.5, -3.5)	-5.1 (-6.5, -3.5)
Min, Max	-9.0, 2.0	-8.0, -1.8
Site 2		
n	28	24
Mean ± SD	-4.9 ± 2.6	-5.1 ± 2.1
Median (p25, p75)	-4.3 (-7.3, -3.0)	-5.0 (-6.8, -3.0)
Min, Max	-10.0, 0.0	-10.0, -2.0
Site 3		
n	18	18
Mean ± SD	-4.2 ± 2.8	-2.9 ± 1.5
Median (p25, p75)	-4.0 (-5.0, -2.0)	-2.8 (-4.0, -2.0)
Min, Max	-10.0, 0.0	-6.0, -0.5
Site 4		
n	15	16
Mean ± SD	-3.4 ± 1.3	-4.8 ± 1.9
Median (p25, p75)	-3.0 (-4.1, -2.0)	-4.5 (-6.0, -4.0)
Min, Max	-6.5, -2.0	-10.0, -2.0
Site 5		
n	53	54
Mean ± SD	-5.4 ± 2.3	-6.0 ± 2.4
Median (p25, p75)	-5.0 (-7.5, -4.0)	-6.1 (-8.0, -4.0)
Min, Max	-10.0, -0.5	-10.0, -1.0

[1]Worst pain experienced within 1 month of screening visit

Table 21.2: Site Poolability: Change in VAS from baseline[1] to six months post hernia repair: regression model results (ITT set)

Covariate	Parameter Estimate (95% CI)	p-value[2]
Intercept	-5.45 (-6.31, -4.59)	
Site 1	0.60 (-0.64, 1.85)	<.0001
Site 2	0.93 (-0.17, 2.03)	
Site 3	3.21 (1.97, 4.44)	
Site 4	0.63 (-0.78, 2.04)	
Site 5	Reference	

Covariate	Parameter Estimate (95% CI)	p-value[2]
Treatment (Ref=Control)	0.62 (-0.25, 1.49)	0.5970
Site 1*Treatment Arm	-0.78 (-2.41, 0.84)	0.1280
Site 2*Treatment Arm	-0.46 (-1.98, 1.06)	
Site 3*Treatment Arm	-1.90 (-3.63, -0.16)	
Site 4*Treatment Arm	0.83 (-1.01, 2.66)	
Site 5*Treatment Arm	Reference	
Repair Technique: TAPP (Ref=TEP)	-0.69 (-1.46, 0.08)	0.0807
[1]Worst pain experienced within 1 month of screening visit [2]Type III		

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included twenty-four (24) investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A summary of all the clinical studies is presented in Table 22 below.

Table 22: Summary of OUS Supplementary Clinical Data

Study Title	Study Design	Objectives	Subjects	Results
First-In-Market Clinical Study OUS: Mittermair R, Jenic G, Kolenik R, Sorre C. TAPP surgery with mesh fixation and peritoneal closure using n-butyl-2-cyanoacrylate (LiquiBand FIX8®)—initial experience. Eur Surg, 2016; 48, 110.	Prospective case study evaluated pain levels and the feasibility of mesh fixation and peritoneal closure with cyanoacrylate in patients undergoing laparoscopic groin hernia repair. Twenty male patients, aged 18-80 years with direct or indirect hernias as well as bilateral hernias, underwent transabdominal pre-peritoneal (TAPP) surgery with 24 hernia	Pain (VAS) was assessed pre-operatively and post-operatively after 6 days and 3 months. Patients were clinically examined and in case of suspected recurrence or questionable clinical results, sonography was performed additionally. Patient follow-up; 6 days and 3 months.	20 LiquiBand FIX8® (LIQUIFIX FIX8™)	This study showed that TAPP surgery using the adhesive technique with n-butyl cyanoacrylate is suitable for mesh fixation and closure of the peritoneal incision. There was only one adverse event (hematoma) reported at 3 months, a rate of 5% for the study.

	repairs in total carried out. The study was performed at the Medical Centre Klinikum Klagenfurt am Worthersee, Austria.			
OUS Clinical study: Dauser B, Szyszkowitx A, Seitinger G,Herbst F. Fixation of mesh and peritoneal closure using n- butyl cyanoacrylate following laparoscopic inguinal hernia repair. Eur Surg (2016). doi:10.1007/s10353-016- 0450-0	Prospective study to evaluate the feasibility of mesh fixation and peritoneal closure with cyanoacrylate in patients with inguinal or femoral hernias which were surgically treated using a TAPP technique. Thirty-four patients aged 20-82 with a mean age of 57, underwent a total of 40 hernia repairs, Which included 34 primary inguinal, 5 recurrent inguinal and 1 femoral hernia. The study was performed at St John of Gods hospital, Vienna, Austria.	Demographic, peri- and post-operative data was recorded prospectively. Data collected included successful mesh fixation, successful peritoneal closure, number of liquid adhesive drops required, duration of hospital stay, and persistent pain. Patient follow-up; 6 weeks and 12 months.	34 LiquiBand FIX8® (LIQUIFIX FIX8™)	The study authors concluded that mesh fixation was effective, and the closure of the peritoneum is both safe and feasible using the LIQUIFIX FIX8™ device. Success rate for transporous glue fixation of polypropylene mesh was 91.2% (135/148). In three cases, an omega 3 fatty acid-covered mesh was used and fixation with a single liquid anchor was possible in 50.0% (6/12), and therefore the coated mesh was not used any longer. Only one adverse event related to persistent pain was reported, at a rate of 2.9%.
OUS Clinical study: Schmidt, J. Fixation of Titanized mesh with N-Butyl- Cyanoacrylate (Nbca) Using a Novel Device: Biocompatibility and Short-Term Results in Laparoscopic Hernia Repair. JSM Gen Surg Cases Images (2017) 2(2):1026.	Prospective study using LiquiBand FIX8® (LIQUIFIX FIX8™) on titanized meshes in primary inguinal TAPP hernia patients.	Operative and post-operative data collected included conversion to open surgery rate, intra- operative blood loss, post-operative pain and length of post-operative hospital stay was recorded. Statistical analysis was undertaken in the form of mean ± standard deviation or percentages. Differences were analyzed if necessary, by unpaired Student's t-test; a p-value of <0.05 was considered significant. Patients were asked to describe their pain sensations at rest along with physical activity through a VAS scale.	67 LiquiBand FIX8® (LIQUIFIX FIX8™)	The study concluded the combined use of titanized polypropylene mesh with LIQUIFIX FIX8™ for mesh fixation is safe and resulted in positive scores for post-operative comfort and low pain scores measured by VAS. There were no critical incidents related to the use of the device. One patient developed an early recurrence (on the first postoperative day) after a heavy coughing episode. This patient was reoperated via Lichtenstein technique during the same hospital

		Patient follow-up; 1 month, 6 month and 12 months.		stay. There was no incidence of recurrence at the 6- month follow up and no recurrence reported for the 20 patients who reached the 12 month follow up at the time of publication.
OUS Clinical study: Wilson, L. Hickey. Laparoscopic transabdominal preperitoneal (TAPP) groin hernia repair using n-butyl-2- cyanoacrylate (LiquiBand FIX8®) for mesh fixation and peritoneal closure: learning experience during introduction into clinical practice.	Retrospective, single arm analysis of data obtained following a post-market evaluation of LiquiBand FIX8® (LIQUIFIX FIX8™) to investigate the safety and effectiveness of the device.	At 6–8-week follow-up, patients were assessed with regards to post- operative recovery and adverse events including wound healing, wound issues, port site swellings/lumps, groin lumps, seroma, hematoma, recurrence, post-operative pain and return to normal activities. Patient follow-up; 6- 8 week Patient Initiated Follow- up (PIFU) review for 12-month and up to 24 months. Telephone PIFU was performed at 24 months utilizing a questionnaire to assess any symptoms/adverse events.	200 LiquiBand FIX8® (LIQUIFIX FIX8™)	The authors concluded that use of LIQUIFIX FIX8™ for mesh fixation and peritoneal closure in TAPP repair is safe and an effective alternative to tacking techniques. Adverse events were seen in thirteen patients (7% . There was only one adverse event potentially attributable to the use LIQUIFIX FIX8™ for mesh fixation (groin hernia recurrence).
OUS Clinical study: Özveri E, Şanlı DET, Yıldırım D, Gök H, Ertem M. Magnetic resonance visualization of iron loaded meshes in patients with pain after inguinal hernia repair [published online ahead of print, 2020 Mar 12]. Hernia. 2020;10.1007/s10029-020-02168-9. doi:10.1007/s10029-020- 02168-9	A retrospective cohort study evaluated the position and deformation of iron-loaded visible mesh implants using MRI and to correlate MRI findings in patients treated for inguinal hernias with post-surgical chronic pain. 152 LiquiBand FIX8® (LIQUIFIX FIX8™) patients underwent TAPP or TEP procedure using iron-loaded mesh for inguinal hernia repair. 298 patients underwent TEP procedure using a mechanical tacker device.	LiquiBandFIX8® (LIQUIFIX FIX8™) was not directly assessed. Patients underwent check-up at 3 months post-operatively. Patients with ongoing pain at 3 months were asked to complete the Short-form Inguinal pain Questionnaire (sf-IPQ). The sf-IPQ is an instrument for the assessment of groin pain and consists of a 12-point scale with two questions; 1. 'Estimate the worst pain you have felt in the operated groin that you have felt in the past week' and 2. 'If you have experience groin pain to what extent has it limited your ability to perform the following activities?'	152 LiquiBand FIX8® (LIQUIFIX FIX8™)	The authors concluded through further communications that the LIQUIFIX FIX8™ hernia mesh fixation device is safe and effective in inguinal hernia mesh fixation when used during a TAPP and TEP technique with no incidences of recurrence. Through email communication, the author confirmed there were no confirmed cases of recurrence where the LIQUIFIX FIX8™ was used as part of the hernia repair with minimum 6 months follow-up.

		Patient follow-up; 3 months		
OUS Clinical study: Koprivica, R. et Al. Adhesive Techniques for Mesh and Peritoneum Fixation in Laparoscopic Inguinal Hernia Repair. Surgery and Surgical Endoscopy. Vol 2, No 2, Oct 2020, pages 11-16	A prospective study evaluating 20 patients who underwent laparoscopic TAPP inguinal hernia repair. N=10 patients (Group 1) underwent mesh fixation and peritoneal closure with tacks and N=10 patients (Group 2) underwent mesh fixation and peritoneal closure with LiquiBand FIX8® (LIQUIFIX FIX8™).	The performance of mesh fixation and peritoneal closure was recorded. Postoperative pain was measured using a visual analogue scale (VAS) and any early postoperative complications such as hematomas, wound infections, and recurrent hernias, were documented. Statistical analysis was used. Patient follow-up; Day 1, Day 6, and Day 30.	10 LiquiBand FIX8® (LIQUIFIX FIX8™)	During the 30-day follow-up, there were no recurrent hernias, wound infections, or hematomas for LIQUIFIX FIX8™.
OUS Clinical study: Bhoopat T, Chansaenroj P. Comparison of intraocular pressure during laparoscopic totally extraperitoneal (TEP) versus transabdominal preperitoneal (TAPP) inguinal hernia repair. Surg Endosc. 2022 Mar;36(3):2018-2024. doi: 10.1007/s00464-021-08487-x. Epub 2021 Apr 12. PMID: 33844088.	A prospective cohort study to evaluate intraocular pressure during laparoscopic TEP versus TAPP inguinal hernia repair. There were 50 patients in total, with 25 patients in each group (TAPP and TEP). LiquiBand FIX8® (LIQUIFIX FIX8™) was used as part of the procedure for peritoneal closure only.	LiquiBandFIX8® (LIQUIFIX FIX8™) was not directly assessed. The relations between peak inspiratory pressure (PIP), mean arterial pressure (MAP), and end-tidal CO2 (EtCO2) were estimated using ANOVA. Univariate and multivariate analyses were performed to determine the factors associated with intraocular pressure (IOP). Patient follow-up; Intraoperative only. Patient follow-up; 1 month, 3 month and 12 months	25 LiquiBand FIX8® (LIQUIFIX FIX8™)	Although the study did not directly evaluate LIQUIFIX FIX8™, the study did not raise any issues with safety or effectiveness of the LIQUIFIX FIX8™ adhesive at the time of surgery for peritoneal closure following inguinal hernia repair when using a TAPP technique. The study confirmed that all operations were performed without complications. No peritoneal tearing occurred during any procedure.

Additional Clinical Information

As described in Table 22 above, several outside-US clinical studies have been performed with the LiquiBand FIX8® (LIQUIFIX FIX8™) device to support the safety and effectiveness in inguinal hernia mesh fixation and/or peritoneal closure. 504 patients underwent mesh fixation (inguinal or femoral repair) with LiquiBand FIX8® (LIQUIFIX FIX8™) and 348 peritoneal closures were performed with the device outside the US

(OUS). A total of two (0.39%) recurrences were reported across the OUS studies Table 22). The data reflects previous design iterations of the LIQUIFIX device, as well as various mesh types other than polypropylene and polyester. OUS Registry data (141 patients) demonstrated perioperative complication rates and 1- year outcome for LIQUIFIX in open inguinal hernia repair are consistent with other similarly marketed fixation devices. The final Precision device was not used in all cases of open inguinal hernia repair to apply the subject liquid fixation. In addition, OUS perioperative complication rates and 5- year outcomes for laparoscopic inguinal hernia repair with LIQUIFIX device (343 patients) are consistent with other marketed fixation devices.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General and Plastic Surgery Devices, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Non-clinical testing performed during the design and development of the LIQUIFIX devices confirmed the product design specifications and indication for use. In the studies, LIQUIFIX operated as intended; hernia mesh is fixed with adequate tensile strength, as well as sufficient tissue-to tissue fixation strength (peritoneal closure) to meet the intended use.

The US pivotal study met the primary effectiveness endpoint with demonstrated non-inferior improvement in pain of the LIQUIFIX FIX8™ treatment device compared to an absorbable tacker device in both the PP and ITT analyses with a significance at p=<.025.

Secondary endpoints also showed success with non-inferior incidence of hernia recurrence evaluated both at the subject level as well as for rate of successful mesh fixation and rate of successful peritoneal closure at time of surgery. Hernia recurrence rate was evaluated at the subject level in the PP and ITT sets. At 6-month follow- up, hernia recurrence at the subject level in the treatment arm was 0.8% (1) in the PP set and 0.7% (1) ITT sets compared to Control which was 1.5% 2) in the PP set and 1.4% (2) in the ITT set. A comparison of the rate of hernia recurrence at each timepoint from 2-week to 12-month follow-up showed a comparable rate between treatment and control. The rate of successful mesh fixation was 100% in both the treatment and control groups. The rate of successful peritoneal closure was also non-inferior, with a mean difference of -2.1% p=0.006) in the PP set and -4.1% (p=0.012) in the ITT set.

Quality of life as assessed by the Carolina Comfort Scale (CCS) questionnaire score showed improvement across the timepoints in the total, sensation and pain domains and the change

was comparable between the treatment and control groups. Pain assessed by VAS improved over the timepoints post-surgery and was similar when the cohorts were compared. Pain in both VAS and the CCS score correlated, both improving over the post-surgical period.

B. Safety Conclusions

The risks of the LIQUIFIX devices are based on non-clinical laboratory (including biocompatibility, chemical characterization, and simulated use testing) and animal studies as well as data collected in OUS and US clinical studies conducted to support PMA approval as described above. The results of this testing support that the use of LIQUIFIX adhesive in hernia mesh fixation and peritoneal closure is safe.

An evaluation of the adverse events in the pivotal study demonstrated that the safety profile of the LIQUIFIX FIX8™ treatment device was comparable to the Control device. The overall incidence of adverse events in the LIQUIFIX FIX8™ treatment arm (114 AEs; 11 SAEs) was lower compared to the control (157 AEs; 16 SAEs). The incidence of possibly device-related AEs by subject was comparable in the treatment 34; 23.9%) and control (43; 30.3%) groups. There were no device or procedure related deaths or unanticipated adverse device effects. No device deficiencies resulted in adverse events at time of surgery.

In terms of SAEs, the incidence of possibly device-related events was comparable between the treatment and control groups. There were 5 events in 5 3.5%) subjects of device related SAEs in the treatment group compared to 4 events in 4 (2.8%) subjects in the control group. For total SAE, within the first 30 days of surgery, 13 (4.6%) subjects presented an SAE (4 LIQUIFIX FIX8™; 9 Control), and in the 31 to 365 days post procedure period, there were 14 (4.9%) subjects (7 LIQUIFIX FIX8™; 7 Control). The most frequent possibly device related serious AEs were the following: Hematoma (0 LIQUIFIX FIX8™; 2 control), inguinal hernia (1 LIQUIFIX FIX8™; 1 control) and neuralgia (2 LIQUIFIX FIX8™; 0 control). All three hernia recurrences recorded in the Study were onset in the 31 to 365 days post procedure period (2 Control, 1 LIQUIFIX FIX8™).

Seroma was the most frequent non-serious AE occurring within 30 days of surgery with 17 events in 16 (11.3%) subjects in the LIQUIFIX FIX8™ group and 26 events in 24 (16.9%) subjects in the control group. All cases were mild in severity. Of all 44 subjects who experienced seroma within the study, nineteen (19) of these seroma events were considered possibly related to device and procedure in the LIQUIFIX FIX8™ treatment group and twenty-five (25) in the control group. Other notable frequent non-serious AEs were groin pain with eighteen (18) events in total, and fourteen (14) of which considered possibly device related (4 LIQUIFIX FIX8™ subjects; 10 Control subjects).

In the 7 OUS studies submitted, risks did not differ from standard of care fixation significantly. A total of 504 patients underwent mesh fixation (inguinal or femoral repair) with LiquiBand FIX8® (LiquiFix FIX8™) and 348 peritoneal closures were performed with the device in laparoscopic surgeries OUS. A total of two 0.39%) recurrences were reported across the OUS studies. OUS Registry data (141 patients) demonstrated perioperative complication rates and 1- year outcome for LiquiFix in open inguinal hernia

repair are consistent with other similarly marketed fixation devices. The final Precision device was not used in all cases of open inguinal hernia repair to apply the subject liquid fixation. However, the applicator difference is not likely to influence the placement of the chemical anchors of LiquiFix in the open anterior inguinal hernia repair on the same tissue, same mesh types and same restricted anatomic space for both the laparoscopic and anterior open repair approaches.

In the clinical studies, type, frequency and severity of adverse events observed across the US clinical study is consistent with that for typical inguinal/femoral hernia mesh fixation repairs and that observed in the Outside US groin hernia repair clinical studies with the LIQUIFIX FIX8™ device.

C. Benefit-Risk Determination

The probable benefits and risks of the device are based on data collected in the US IDE clinical study conducted to support PMA approval as described above as well as seven (7) OUS clinical studies and Real World Evidence from 141 OUS registry patients to supplement this data.

The probable benefit outweighs the risks for most patients. The US pivotal study demonstrated that LIQUIFIX FIX8™ is non-inferior to control (US marketed tacker device) in terms of improvement in pain at 6 months, incidence of hernia recurrence at 12 months and rate of successful mesh fixation and peritoneal closure at time of surgery. Patient perspectives considered during the review included quality of life throughout follow-up.

In terms of safety outcomes, the incidence of device related adverse events were comparable in the LIQUIFIX FIX8™ and control group. Although not statistically powered, the Outside US prospective studies showed similar results; Observed adverse events were similar (e.g., chronic pain, hematoma, recurrence, seroma and urinary retention) to that recorded in the US pivotal study. The US pivotal study device did not present any unknown risks that have not been previously described.

Based on these results, there is an overall benefit to the availability of a device that provides an atraumatic surgical adhesive for the repair of groin hernias as an alternative to penetrative mechanical tackers. As a non-penetrative device, LIQUIFIX FIX8™ is not restricted in terms of location of application on mesh, whereas the tacker devices are more limited to where it can be applied due to its penetrative nature. Using glue instead of mechanical mesh fixation methods aims to avoid the trauma associated with tissue penetration.

In conclusion, given the available information, the data support LIQUIFIX FIX8™ and LIQUIFIX Precision™ Open for the use in surgical repair of groin (inguinal and femoral) hernias, achieved through the fixation of prosthetic polypropylene and polyester mesh to the abdominal wall and the approximation of the peritoneum, the probable benefits outweigh the probable risks.

There are limitations to these conclusions. First, the data from the German hernia registry on open inguinal hernia repair consisted of summary, high-level conclusions. Mesh fixation in open inguinal hernia repair with LiquiFix Precision demonstrated similar recurrence rates and adverse events as standard of care. Granular data on use of LiquiFix in open hernia repair was not available, and long-term data on minimally invasive inguinal hernia repair beyond 1 year was not studied in the U.S. clinical study. For these reasons, a post-market study will be requested from the sponsor to address these issues. Furthermore, training will be required of the user with assessment of their understanding of the label prior to use of the device. This is intended to mitigate the risk of device dripping outside the area of mesh fixation, to ensure adequate device polymerization for mesh fixation, and to prevent applicator clogging. Clogging of the applicator was the most frequent device malfunction sited in the U.S. studies.

1. Patient Perspective
   Patient perspectives considered during the review included quality of life (QOL) throughout follow-up. QOL was assessed at each post-operative follow-up visit using a Carolina Comfort Scale questionnaire, which assessed pain, sensation of mesh, and movement limitations over various activities.

In conclusion, given the available information above, the data support that for repair of groin (femoral and inguinal) hernias, achieved through the fixation of prosthetic polypropylene or polyester mesh to the abdominal wall, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the LIQUIFIX devices when used in accordance with the indications for use.
The results of the study confirm the safety and effectiveness of the LIQUIFIX adhesive for use in mesh fixation for the surgical repair of groin (inguinal and femoral) hernias and where applicable, peritoneal closure (TAPP). The primary effectiveness endpoint was met with non-inferior improvement in pain compared to control. Secondary endpoints related to hernia recurrence, successful mesh fixation and successful peritoneal closure were also met. Improvement in quality of life and overall pain were comparable to control. The safety profile was confirmed as acceptable when compared to the control device. Data gaps in the use of LiquiFix in open inguinal hernia repair and long-term data beyond 12 months on adverse events occurring as a result of the non-absorbability of the LiquiFix anchor will require a post approval study (PAS). The study will focus on long-term, device-related adverse events, such as chronic pain, hernia recurrence, delayed mesh infection, and mesh migration with erosion into critical anatomic structures. The PAS will also enroll patients undergoing open inguinal hernia repair with use of LiquiFix for mesh fixation when placed in an onlay fashion on the floor of the inguinal canal. The PAS will be requested as a condition of device approval.

XIV. CDRH DECISION

CDRH issued an approval order on June 2, 2023. The final clinical conditions of approval cited in the approval order are described below.

1. Post Approval Study

You must obtain approval of your post-approval study (PAS) protocol(s) within 60 days from the date of this order. Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes a complete protocol of your post-approval study described below. Your PMA supplement should be clearly labeled as a "PMA Post-Approval Study Protocol" as noted below and submitted to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below.

The LiquiFix Post-Approval Study

Per agreement reached on May 26, 2023 (email), this study is an observational study to evaluate the long-term safety of the LiquiFix devices using real-world evidence methods. Study participants will include all U.S. patients undergoing open and laparoscopic inguinal/femoral hernia repair who are treated within the first year or a minimum of 206 patients for LiquiFix Precision Open and 103 LiquiFix FIX8, whichever is largest, that are entered into the Abdominal Core Health Quality Collaborative (ACHQC) as well as continued follow-up of the available IDE patients currently enrolled in the ACHQC. Endpoints will include:

- Recurrence – as measured by ACHQC questionnaire, the validated questionnaire by Tastaldi, et al, as used for virtual visits in the IDE study
- Mesh excision – as measured by ACHQC questionnaire
- Infection – as measured by ACHQC questionnaire
- Pain – as measured by Visual Analog Scale (VAS)
- Quality of Life – as assessed by questionnaire
- Complications – as measured by ACHQC questionnaire

The rate of hernia recurrence, rate of adverse events (specifically bowel obstruction, infection, and mesh migration) will be compared to pre-specified performance goals or a control. Acute and long-term safety of the LiquiFix device will be evaluated annually for minimum 2 years post-surgery.

From the date of study protocol approval, you must meet the following timelines for the LiquiFix PAS:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, you must submit separate periodic reports on the progress of the PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

2. <u>Device-Specific Training Program</u>

1) The device manufacturer must develop, maintain, and update as necessary, a device-specific use training program that ensures proper training in use of the device for open and minimally invasive procedures, proper dispensation and use of the applicator, identification and management of potential adverse events, including misapplication and removal of product applied to or located on the wrong tissues or anatomic structures.

2) The device-specific use training program is submitted, as a supplement, within 30 days from the date of the approval letter and approved by FDA prior to implementation.

3) The device-specific use training program is implemented within 6 months from the date of the approval letter. A report must be submitted to FDA within 30 days of implementation to notify FDA of this milestone.

4) The device manufacturer will proactively make available all training content to each facility requesting to order the product.

5) The device manufacturer must submit a report to the FDA annually on the anniversary of initial marketing authorization for the device, until such time as FDA may terminate such reporting, the number of providers who have completed the training with LiquiFix representatives, the number of new facilities ordering the device, and any changes to the training program since the last report.

6) The device manufacturer will include in the labeling a statement that use of the device is limited to those healthcare providers who are qualified to perform open or laparoscopic hernia repairs and that only physicians having adequate training and familiarity with surgical techniques should use the device.

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES